

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 15 December 1999 (15.12.99)		
International application No. PCT/CA99/00375	Applicant's or agent's file reference 3206-169	
International filing date (day/month/year) 27 April 1999 (27.04.99)	Priority date (day/month/year) 27 April 1998 (27.04.98)	
Applicant		
EGAN, Sean, E. et al		

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

16 November 1999 (16.11.99)

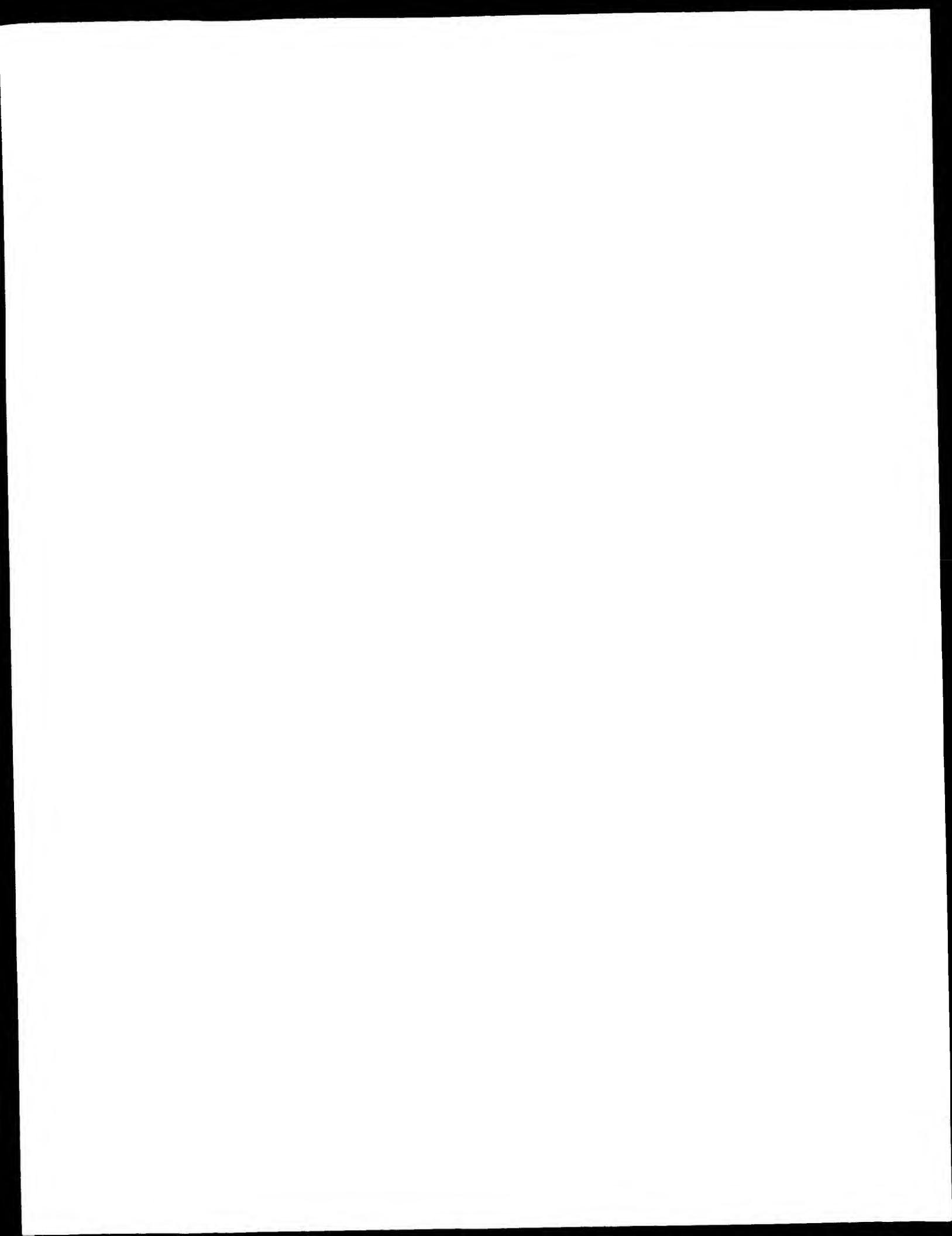
in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38



BM

PATENT COOPERATION TREATY

PCT

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and
Administrative Instructions, Sections 402 and 409)

Date of mailing (day/month/year)
29 July 1999 (29.07.99)

From the INTERNATIONAL BUREAU

To:

RAE, Patricia, A.
Sim & McBurney
6th Floor
330 University Avenue
Toronto, Ontario M5G 1R7
CANADA

Applicant's or agent's file reference
3206-169

IMPORTANT NOTIFICATION

International application No.
PCT/CA99/00375

International filing date (day/month/year)
27 April 1999 (27.04.99)

Applicant

HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP et al

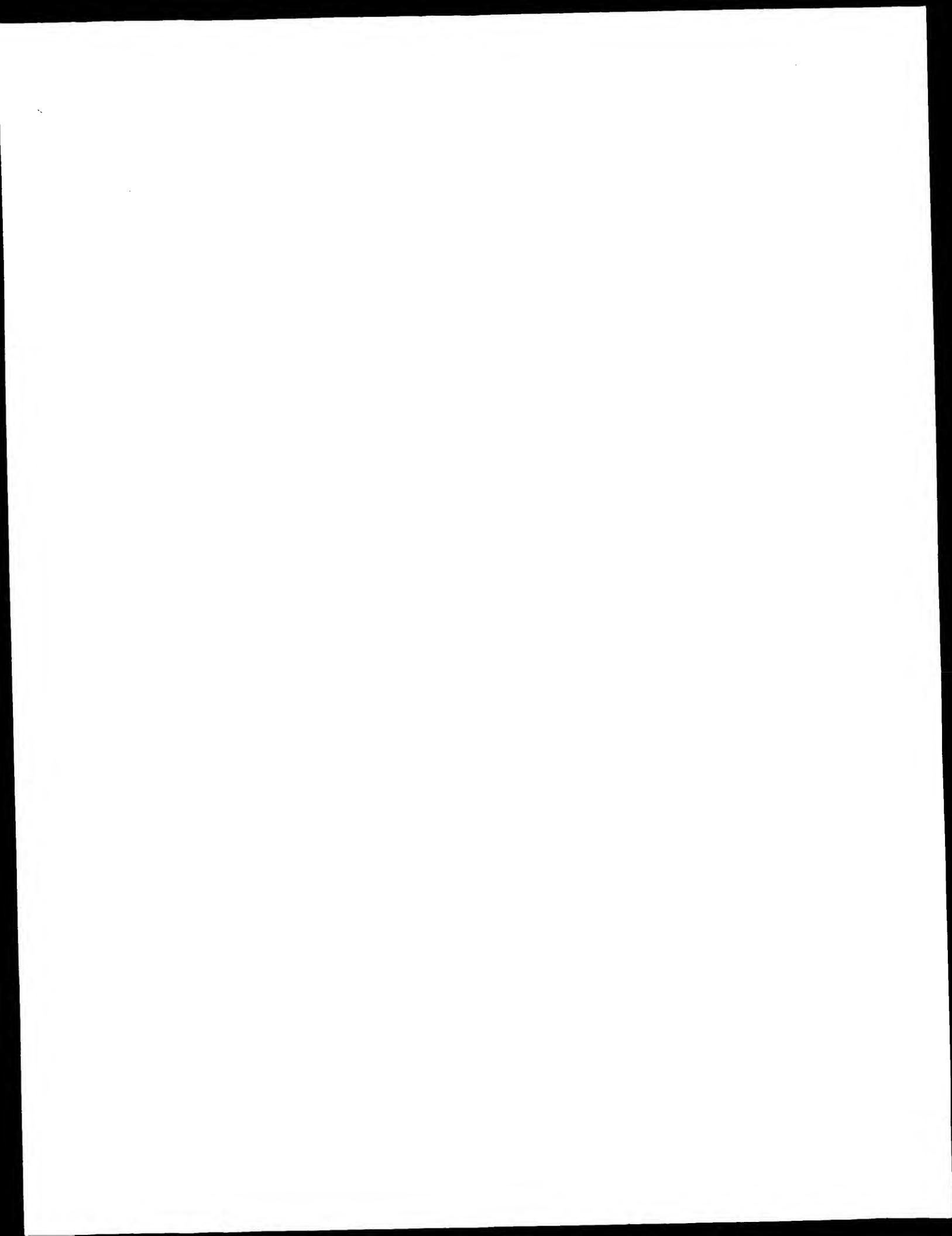
The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. **Correction of priority claim.** In accordance with the applicant's notice received on: 15 July 1999 (15.07.99), the following priority claim has been corrected to read as follows:
US 05 February 1999 (05.02.99) 60/118,739
 - even though the indication of the number of the earlier application is missing.
 - even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:
2. **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:
 - even though the indication of the number of the earlier application is missing.
 - even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:
3. As a **result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:
4. **Priority claim considered not to have been made.**
 - The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
 - The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
 - The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(1B).
5. In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim(s):
US 05 February 1999 (05.02.99) 60/118,739
6. A copy of this notification has been sent to the receiving Office and
 - to the International Searching Authority (where the international search report has not yet been issued).
 - the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer
Facsimile No. (41-22) 740.14.35	Ting Zhao
Form PCT/IB/318 (July 1998)	Telephone No. (41-22) 338.83.38

002760928

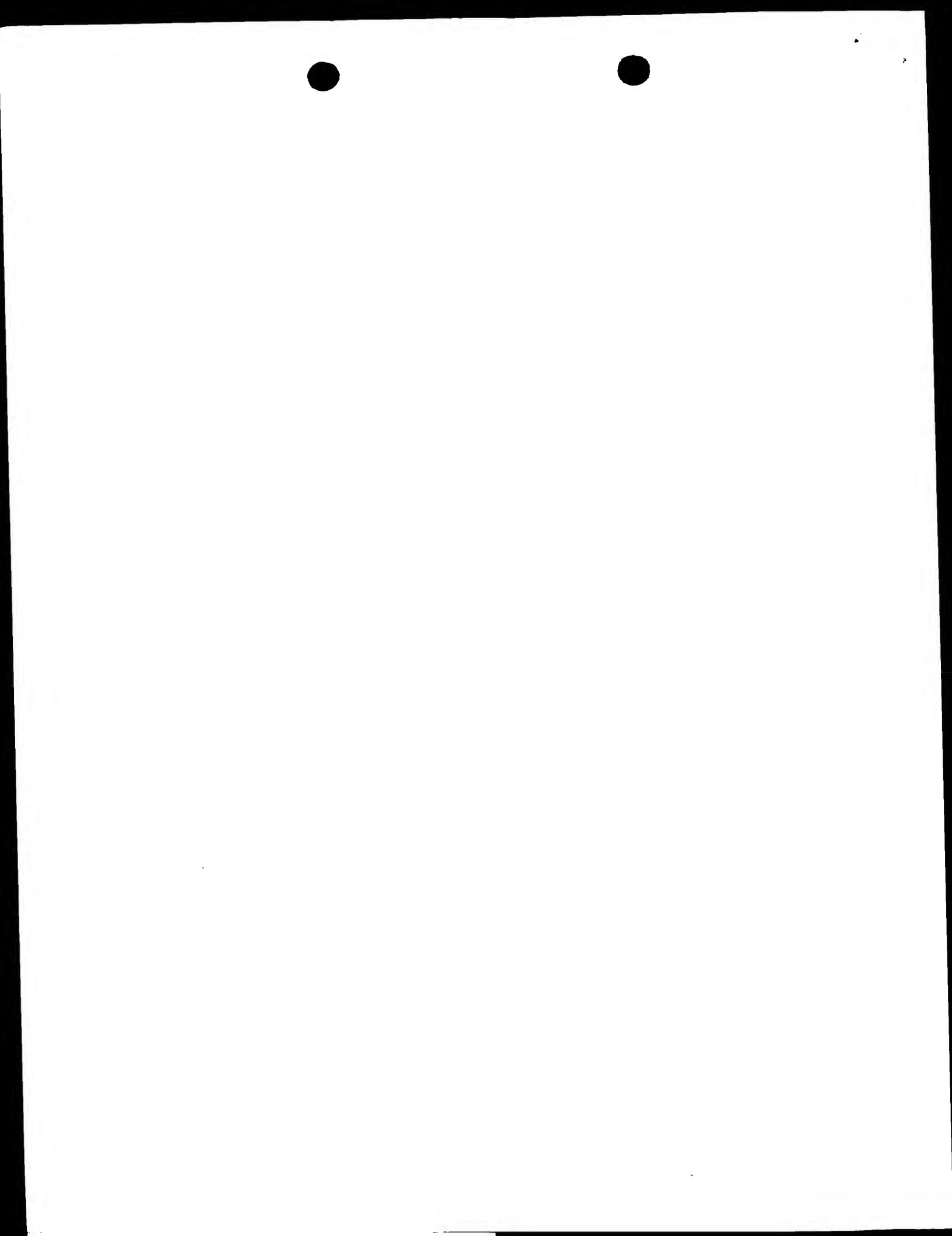


PCT REQUEST

Original (for SUBMISSION) - printed on 27.04.1999 04:18:43 PM

3206-169

0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request Prepared using	
0-4-1	PCT-EASY Version 2.83 (updated 01.03.1999)	
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	
0-7	Applicant's or agent's file reference	
I	Title of invention	
II	Applicant	
II-1	This person is:	
II-2	Applicant for	
II-4	Name	
II-5	Address:	
II-6	State of nationality	
II-7	State of residence	
II-8	Telephone No.	
II-9	Facsimile No.	
III-1	Applicant and/or inventor	
III-1-1	This person is:	
III-1-2	Applicant for	
III-1-4	Name (LAST, First)	
III-1-5	Address:	
III-1-6	State of nationality	
III-1-7	State of residence	

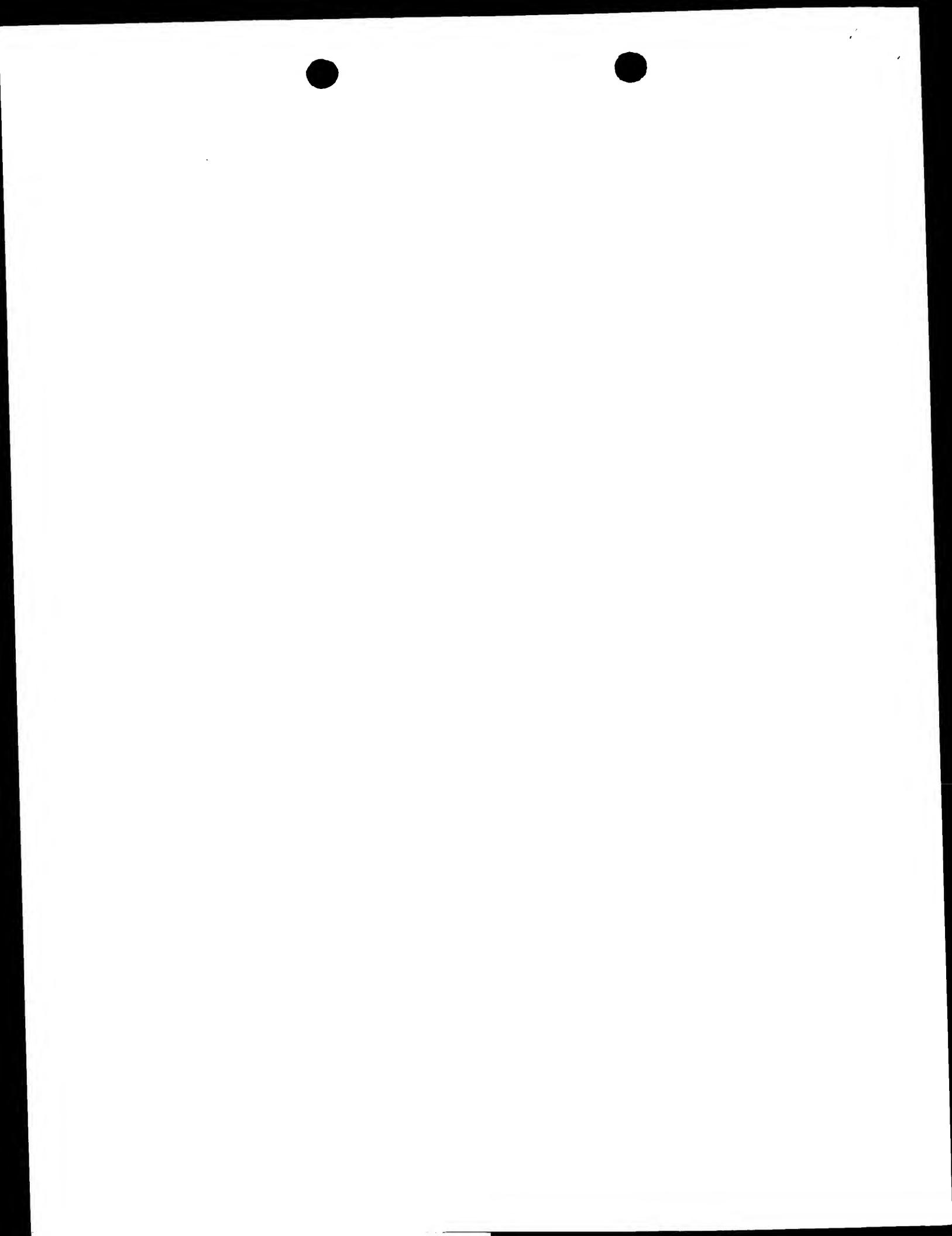


PCT REQUEST

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3206-169

III-2	Applicant and/or inventor	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	WANG, Wei
III-2-5	Address:	THE HOSPITAL FOR SICK CHILDREN 555 University Avenue Toronto, Ontario M5G 1X8 Canada
III-2-6	State of nationality	CA
III-2-7	State of residence	CA
III-3	Applicant and/or inventor	
III-3-1	This person is:	applicant and inventor
III-3-2	Applicant for	US only
III-3-4	Name (LAST, First)	SENGAR, Ameet
III-3-5	Address:	THE HOSPITAL FOR SICK CHILDREN 555 University Avenue Toronto, Ontario M5G 1X8 Canada
III-3-6	State of nationality	CA
III-3-7	State of residence	CA
IV-1	Agent or common representative; or address for correspondence	
	The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent international Authorities as:	agent
IV-1-1	Name (LAST, First)	RAE, Patricia, A.
IV-1-2	Address:	Sim & McBurney 330 University Avenue 6th Floor Toronto, Ontario M5G 1R7 Canada
IV-1-3	Telephone No.	416-595-1155
IV-1-4	Facsimile No.	416-595-1163

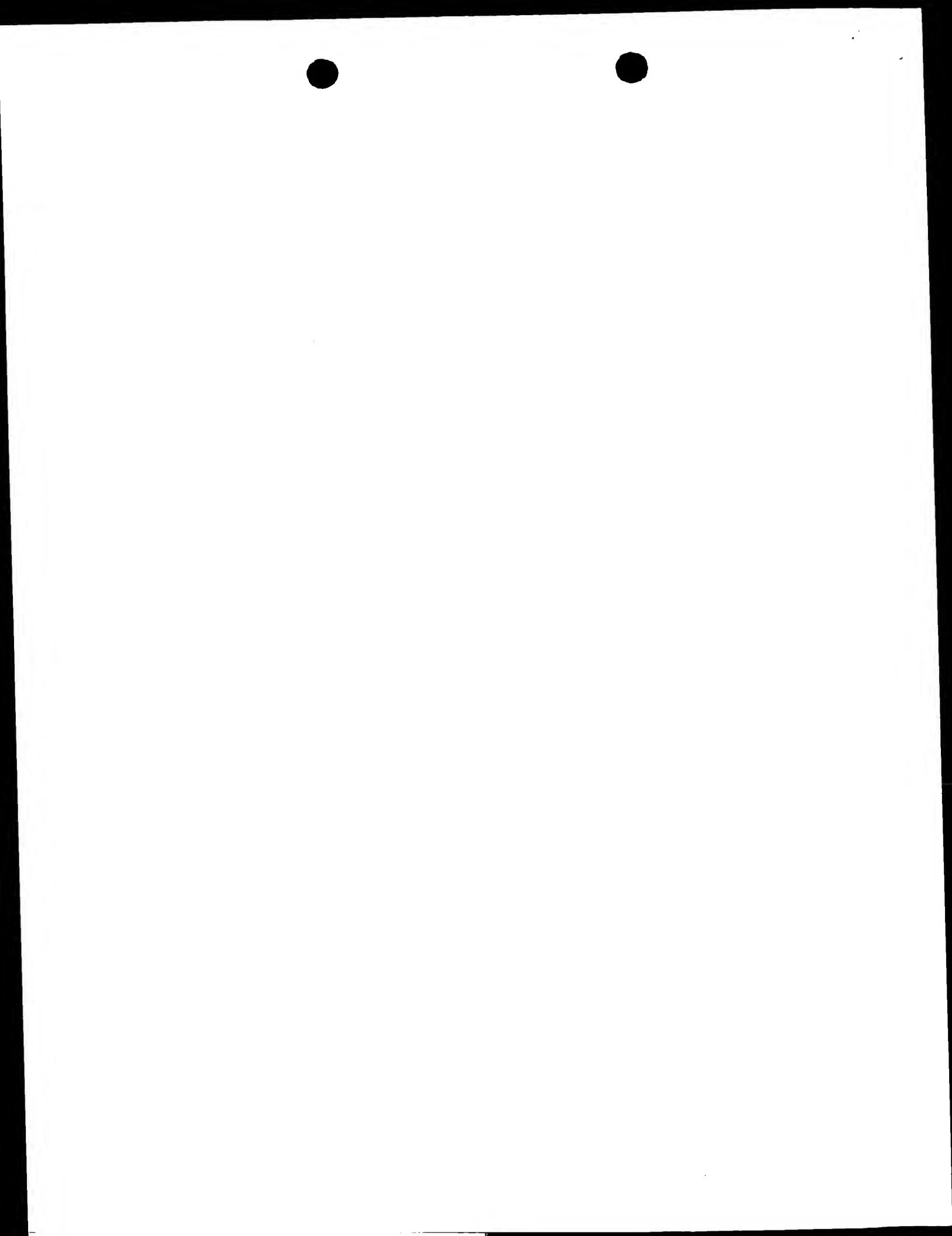


PCT REQUEST

Original (for SUBMISSION) - printed on 27.04.1999 04:18:43 PM

3206-169

V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW SD SZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AL AM AT AU AZ BA BB BG BR BY CA CH&LI CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
V-5	Precautionary Designation Statement In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	Exclusion(s) from precautionary designations	NONE
VI-1	Priority claim of earlier national application	
VI-1-1	Filing date	27 April 1998 (27.04.1998)
VI-1-2	Number	2,230,201
VI-1-3	Country	CA
VI-2	Priority claim of earlier national application	
VI-2-1	Filing date	02 February 1999 (02.02.1999)
VI-2-2	Number	60/118,739
VI-2-3	Country	US



PCT REQUEST

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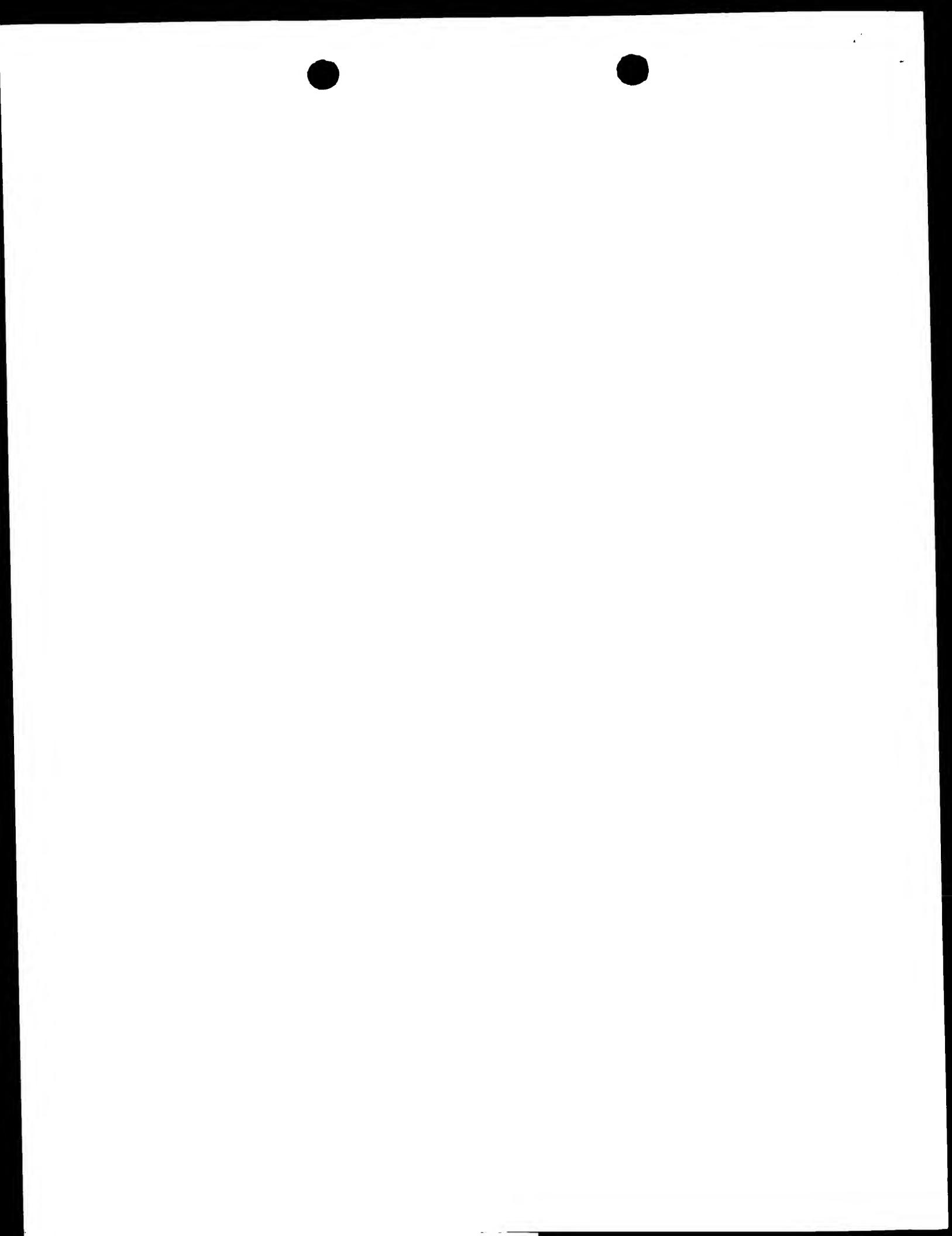
VI-3	Priority document request The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1	
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)	
VIII	Check list	number of sheets	electronic file(s) attached
VIII-1	Request	4	-
VIII-2	Description	76	-
VIII-3	Claims	6	-
VIII-4	Abstract	1	abstract.txt
VIII-5	Drawings	7	-
VIII-7	TOTAL	94	
VIII-8	Accompanying items Fee calculation sheet	paper document(s) attached	electronic file(s) attached
VIII-16	PCT-EASY diskette	✓	-
VIII-18	Figure of the drawings which should accompany the abstract	Fig. 1	
VIII-19	Language of filing of the international application	English	
IX-1	Signature of applicant or agent	<i>Patricia Lee</i>	
IX-1-1	Name (LAST, First)	RAE, Patricia, A.	

FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	
10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
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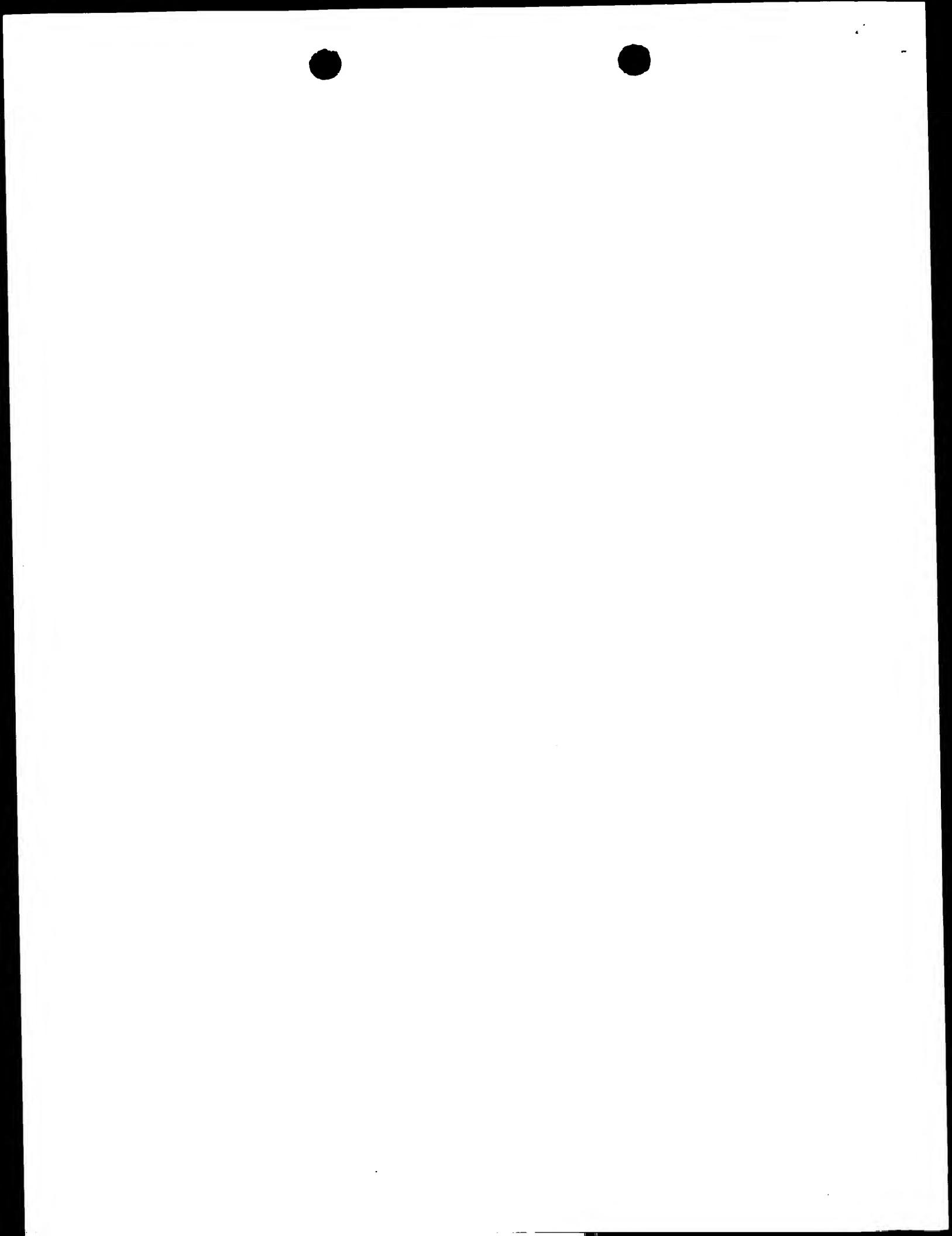
PCT (ANNEX - FEE CALCULATION SHEET)

Original (for SUBMISSION) - printed on 27.04.1999 04:18:43 PM

3206-169

(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only		
0-1	International Application No.		
0-2	Date stamp of the receiving Office		
0-4	Form - PCT/RO/101 (Annex) PCT Fee Calculation Sheet Prepared using	PCT-EASY Version 2.83 (updated 01.03.1999)	
0-9	Applicant's or agent's file reference	3206-169	
2	Applicant	HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP, et al.	
12	Calculation of prescribed fees	fee amount/multiplier	total amounts (CAD)
12-1	Transmittal fee	T	⇒ 200
12-2	Search fee	S	⇒ 2,088
12-3	International fee		
12-4	Basic fee (first 30 sheets)	b1	721
12-5	Remaining sheets		64
12-6	Additional amount	(X)	17
12-7	Total additional amount	b2	1,088
12-8	b1 + b2 =	B	1,809
12-9	Designation fees		
12-10	Number of designations contained in international application		79
12-11	Number of designation fees payable (maximum 10)		10
12-12	Amount of designation fee	(X)	166
12-13	Total designation fees	D	1,660
12-14	PCT-EASY fee reduction	R	-220
12-15	Total International fee (B+D-R)	I	⇒ 3,249
12-16	Fee for priority document		
12-17	Number of priority documents requested		1
12-18	Fee per document	(X)	63
12-19	Total priority document fee	P	⇒ 63
12-20	TOTAL FEES PAYABLE (T+S+I+P)		⇒ 5,600
12-21	Mode of payment	cheque	
12-22	Deposit account instructions The receiving Office:	Canadian Patent Office (RO/CA)	
12-23	is hereby authorized to charge any deficiency or credit any over-payment in the total fees indicated above to my deposit account	✓	
12-24	is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account	✓	



PCT (ANNEX - FEE CALCULATION SHEET)

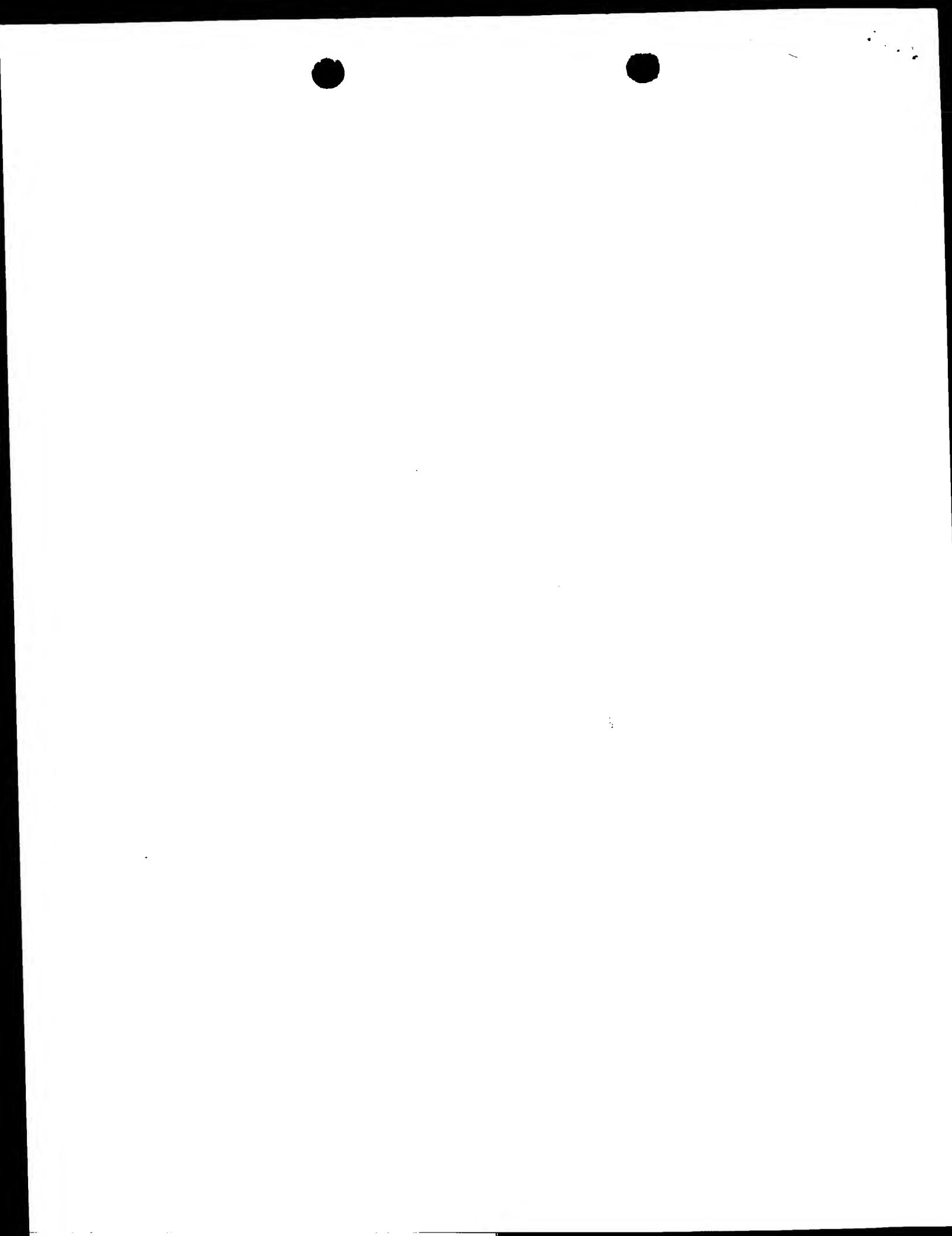
Original (for SUBMISSION) - printed on 27.04.1999 04:18:43 PM

3206-169

12-21	Deposit account No.	000000000
12-22	Date	27 April 1999 (27.04.1999)
12-23	Name and signature	RAE, Patricia, A.

VALIDATION LOG AND REMARKS

13-2-6	Validation messages Contents	<p>Yellow!</p> <p>The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.</p>
		<p>Green?</p> <p>Priority 2. The priority document is not enclosed. (The applicant must furnish it within 16 months from the earliest priority date claimed)</p>

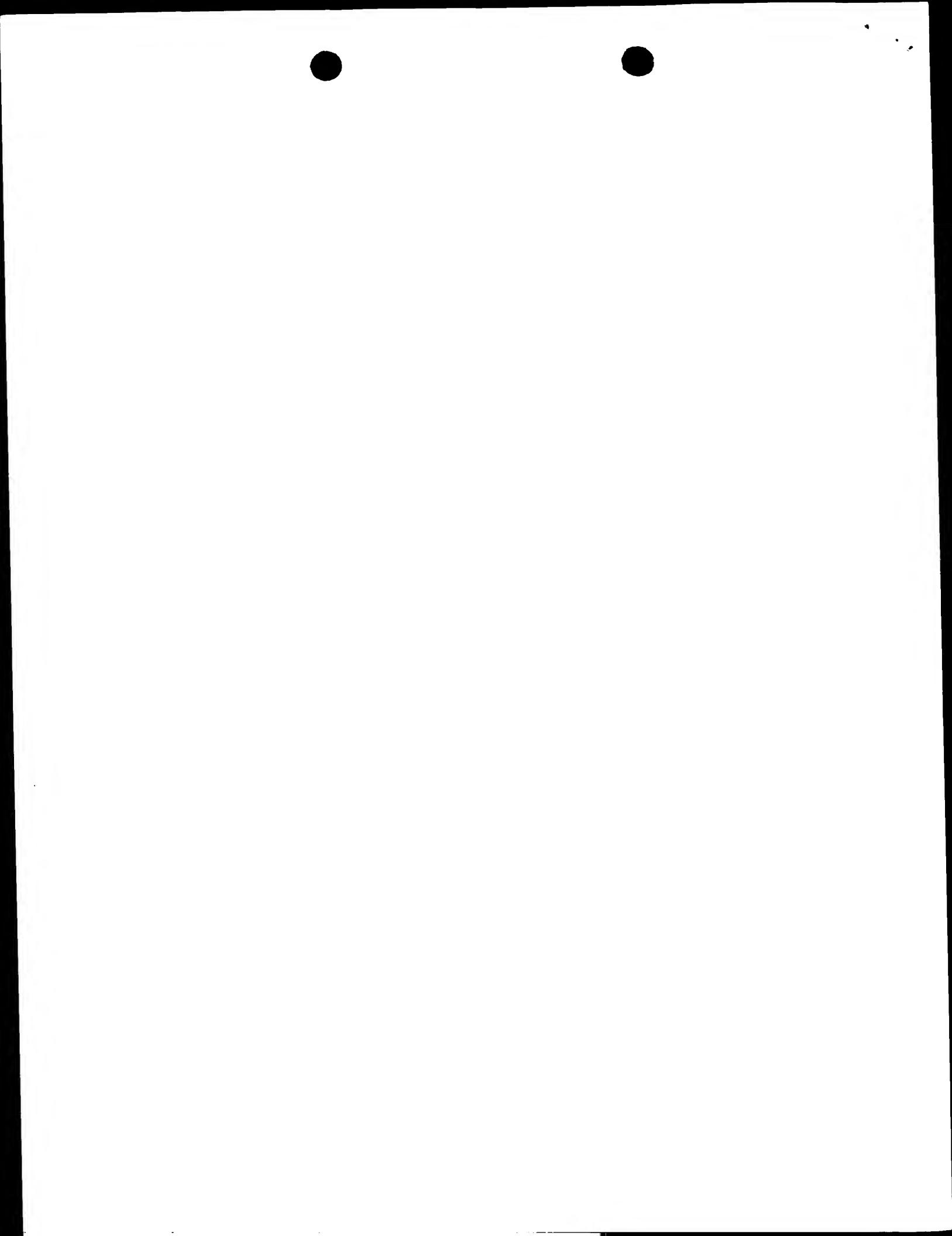


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FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No.	PCT/CA99/00375	For International Preliminary Examining Authority use only								
Applicant's or agent's file reference	3206-169 PAR	Date stamp of the IPEA								
<p>Applicant HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP et al.</p>										
<p>Calculation of prescribed fees</p>										
<p>1. Preliminary examination fee 2,998.29 P</p>										
<p>2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>) 289.46 H</p>										
<p>3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box 3,287.75 TOTAL</p>										
<p>Mode of Payment</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;"><input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)</td> <td style="width: 50%;"><input type="checkbox"/> cash</td> </tr> <tr> <td><input type="checkbox"/> cheque</td> <td><input type="checkbox"/> revenue stamps</td> </tr> <tr> <td><input type="checkbox"/> postal money order</td> <td><input type="checkbox"/> coupons</td> </tr> <tr> <td><input checked="" type="checkbox"/> bank draft</td> <td><input type="checkbox"/> other (<i>specify</i>): _____</td> </tr> </table>			<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash	<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps	<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons	<input checked="" type="checkbox"/> bank draft	<input type="checkbox"/> other (<i>specify</i>): _____
<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash									
<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps									
<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons									
<input checked="" type="checkbox"/> bank draft	<input type="checkbox"/> other (<i>specify</i>): _____									
<p>Deposit Account Authorization (<i>this mode of payment may not be available at all IPEAs</i>)</p> <p>The IPEA/ <u> </u> <input type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.</p> <p><input type="checkbox"/> (<i>this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit</i>) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.</p>										
Deposit Account Number	Date (day/month/year)	Signature								



Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is agent common representative

and has been appointed earlier and represents the applicant(s) also for international preliminary examination.

is hereby appointed and any earlier appointment of (an) agent(s) /common representative is hereby revoked.

is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official
The address must include postal code and name of country.)*

RAE, Patricia, A.
Sim & McBurney
330 University Avenue
6th Floor
Toronto, Ontario M5G 1R7
Canada

Telephone No.:
(416) 595-1155

Faxsimile No.:
(416) 595-1163

Teleprinter No.:

Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

1. The applicant wishes the international preliminary examination **to start on the basis of:**

the international application as originally filed.

the description as originally filed
 as amended under Article 34

the claims as originally filed
 as amended under Article 19 (together with any accompanying statement)
 as amended under Article 34

the drawings as originally filed
 as amended under Article 34

2. The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. The applicant wishes the start of the international preliminary examination **to be postponed** until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

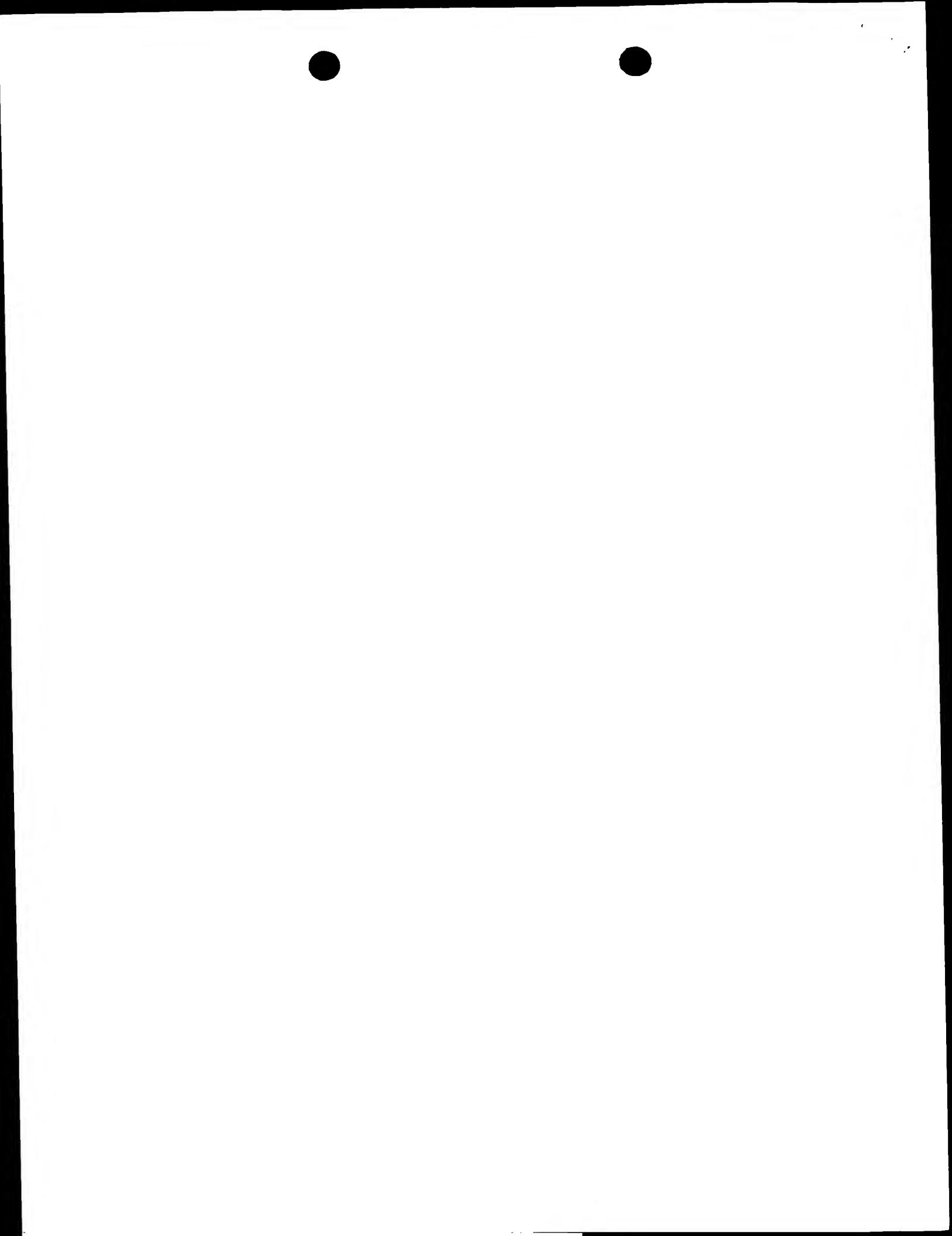
Language for the purposes of international preliminary examination: English

which is the language in which the international application was filed.
 which is the language of a translation furnished for the purposes of international search.
 which is the language of publication of the international application.
 which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby **elects all eligible States** *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes **not to elect**:



Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

1. translation of international application	:	sheets	For International Preliminary Examining Authority use only
2. amendments under Article 34	:	sheets	received <input type="checkbox"/> not received <input type="checkbox"/>
3. copy (or where required, translation) of amendments under Article 19	:	sheets	<input type="checkbox"/> <input type="checkbox"/>
4. copy (or, where required, translation) of statement under Article 19	:	sheets	<input type="checkbox"/> <input type="checkbox"/>
5. letter	:	sheets	<input type="checkbox"/> <input type="checkbox"/>
6. other (specify)	:	sheets	<input type="checkbox"/> <input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

1. <input checked="" type="checkbox"/> fee calculation sheet	4. <input type="checkbox"/> statement explaining lack of signature
2. <input type="checkbox"/> separate signed power of attorney	5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form
3. <input type="checkbox"/> copy of general power of attorney; reference number, if any:	6. <input type="checkbox"/> other (specify):

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

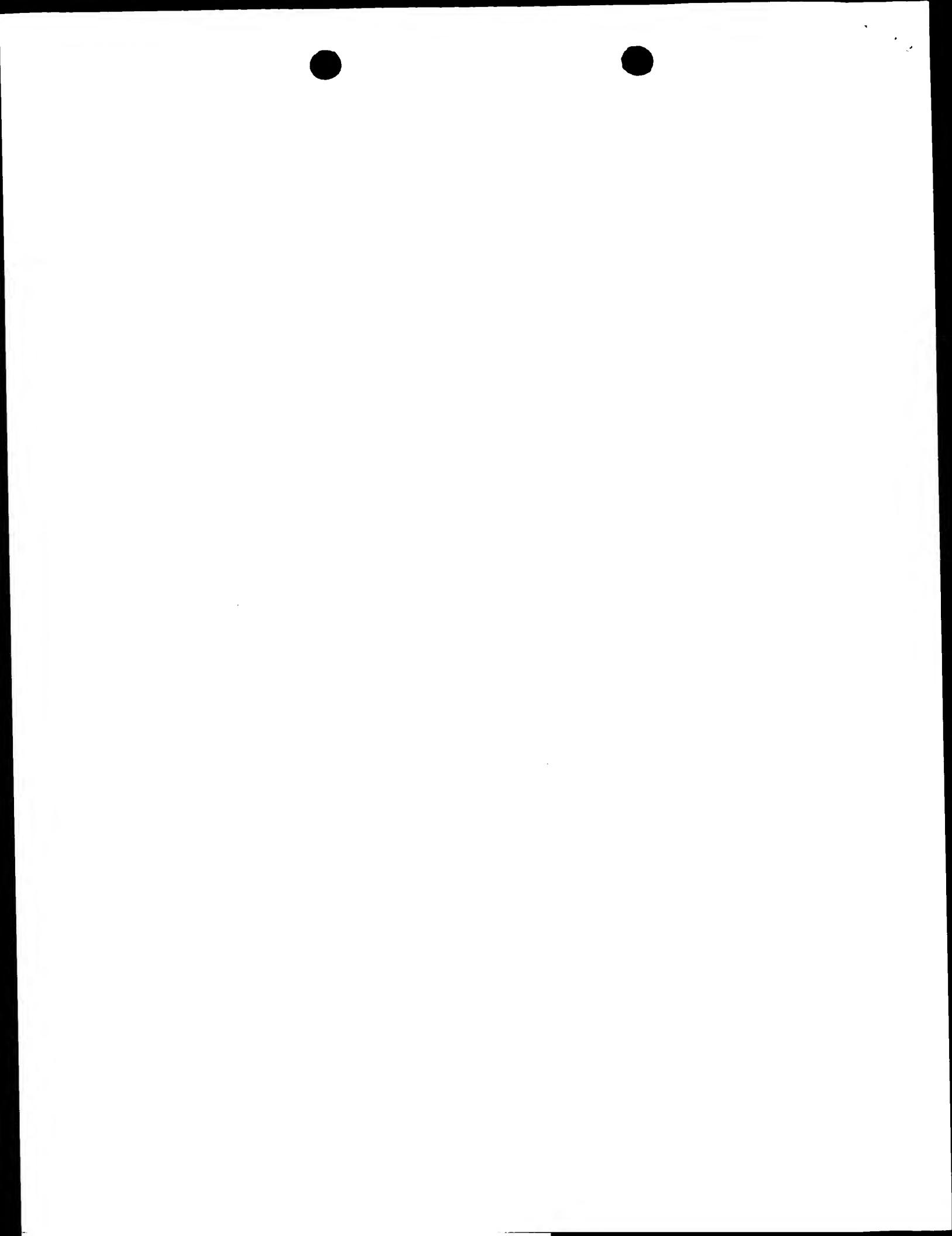
RAE, Patricia A. (Dr.)
Sim & McBurney

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:	<hr/>	
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):	<hr/>	
3. <input type="checkbox"/> The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.	<input type="checkbox"/> The applicant has been informed accordingly.	<hr/>
4. <input type="checkbox"/> The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.	<hr/>	
5. <input type="checkbox"/> Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.	<hr/>	

For International Bureau use only

Demand received from IPEA on:



The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line IPEA/ EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:

The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference 3206-169 PAR
International application No. PCT/CA99/00375	International filing date (day/month/year) 27 April 1999 (27.04.99)	(Earliest) Priority date (day/month/year) 27 April 1998 (27.04.98)
Title of invention ESE GENES AND PROTEINS		
Box No. II APPLICANT(S)		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP 555 University Avenue Toronto, Ontario M5G 1X8 Canada		Telephone No.: (416) 813-1500
		Facsimile No.: (416) 813-5085
		Teleprinter No.:
State (that is, country) of nationality: CA	State (that is, country) of residence: CA	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) EGAN, Sean, E. THE HOSPITAL FOR SICK CHILDREN 555 University Avenue Toronto, Ontario M5G 1X8 Canada		
State (that is, country) of nationality: CA	State (that is, country) of residence: CA	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) WANG, Wei THE HOSPITAL FOR SICK CHILDREN 555 University Avenue Toronto, Ontario M5G 1X8 Canada		
State (that is, country) of nationality: CA	State (that is, country) of residence: CA	
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.		



Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet is not to be included in the demand.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

SENGAR, Ameet
THE HOSPITAL FOR SICK CHILDREN
555 University Avenue
Toronto, Ontario M5G 1X8
Canada

State *(that is, country)* of nationality:
CA

State *(that is, country)* of residence:
CA

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

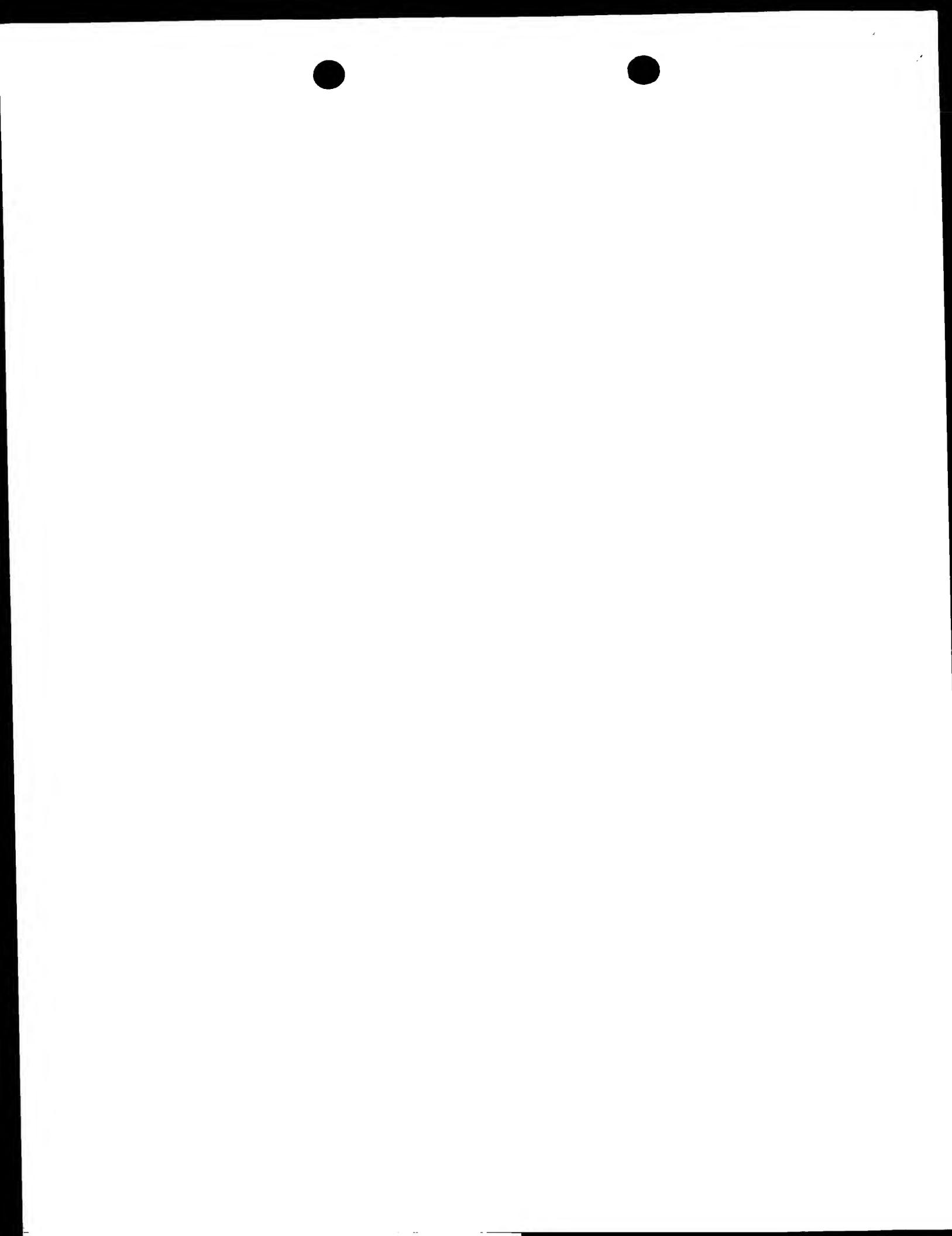
Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:



Further applicants are indicated on another continuation sheet.



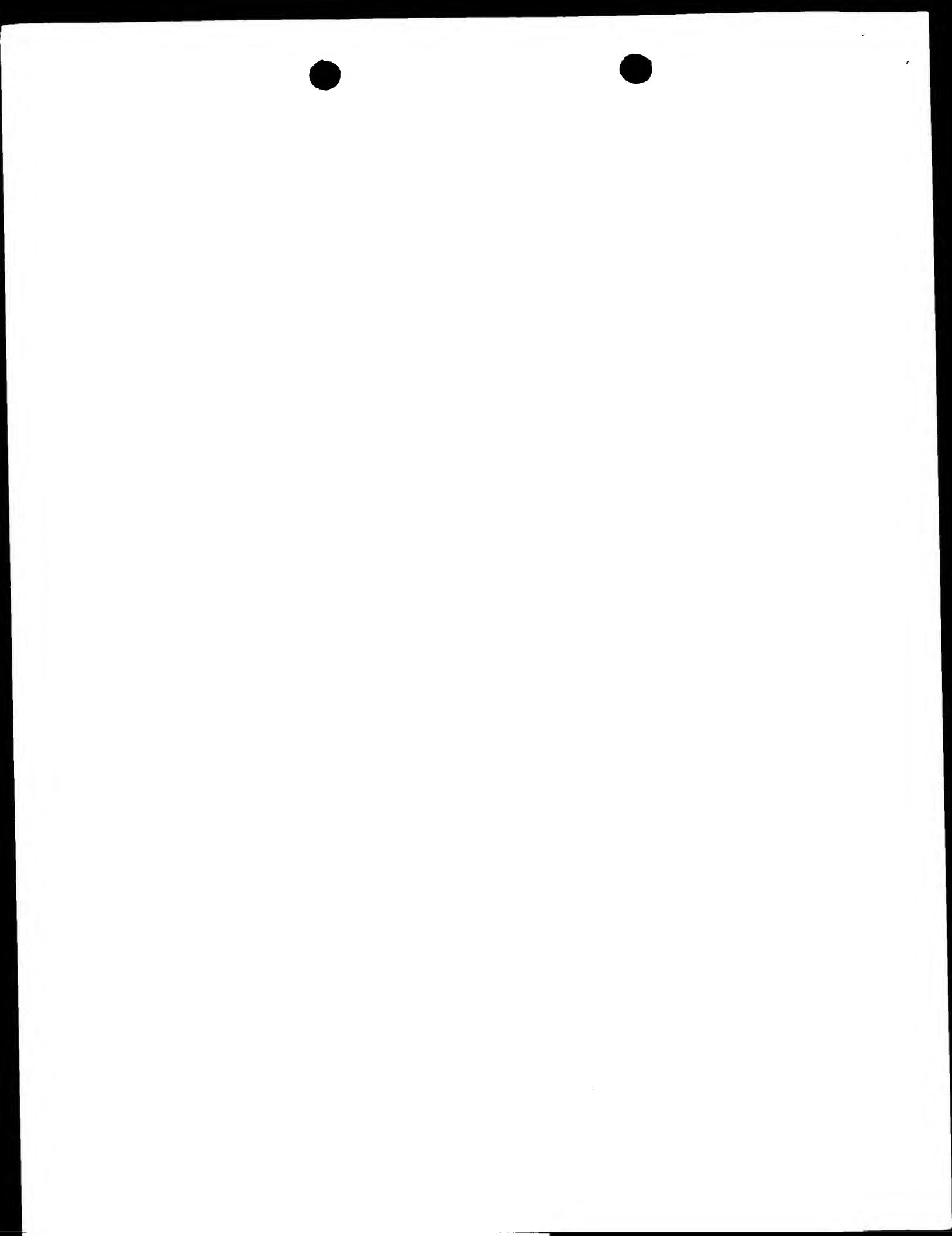
PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3206-169	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CA99/00375	International filing date (day/month/year) 27/04/1999	Priority date (day/month/year) 27/04/1998
International Patent Classification (IPC) or national classification and IPC C12N15/12		
<p>Applicant HSC RESEARCH AND DEVELOPMENT LIMITED...et al.</p> <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 16/11/1999	Date of completion of this report 01.08.2000	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Armandola, E Telephone No. +49 89 2399 7493	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA99/00375

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-82 as originally filed

Claims, No.:

1-49 as originally filed

Drawings, sheets:

1/9-9/9 as originally filed

2. The amendments have resulted in the cancellation of:

the description. pages:
 the claims. Nos.:
 the drawings. sheets:

3. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

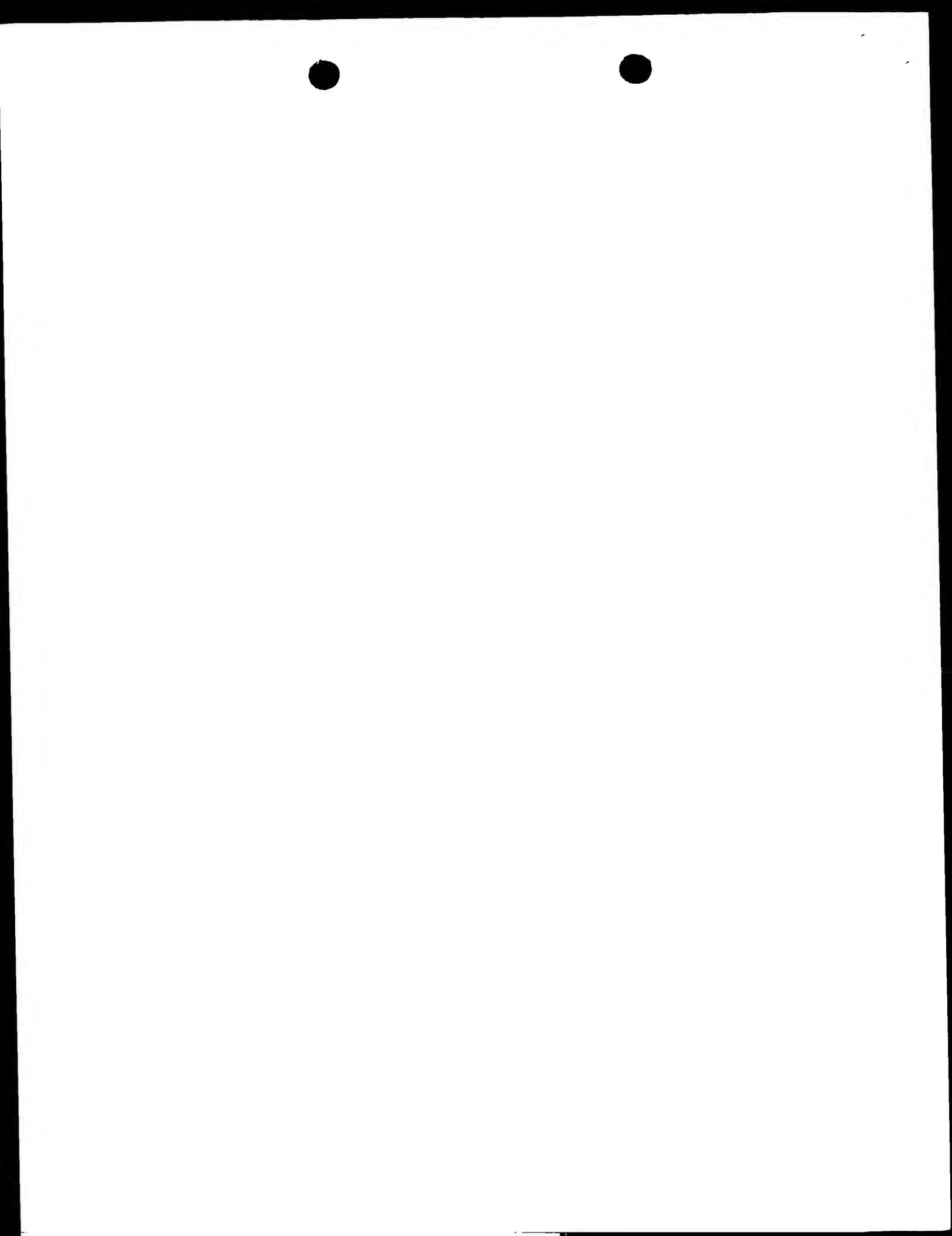
4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.
 claims Nos. 41, 42, 49 (IA): 44-48 (partially) (N, IS, IA).

because:



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the said international application, or the said claims Nos. 41, 42, 44-49 (IA) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. 44-48 (partially).

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

restricted the claims.

paid additional fees.

paid additional fees under protest.

neither restricted nor paid additional fees.

2. This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

complied with.

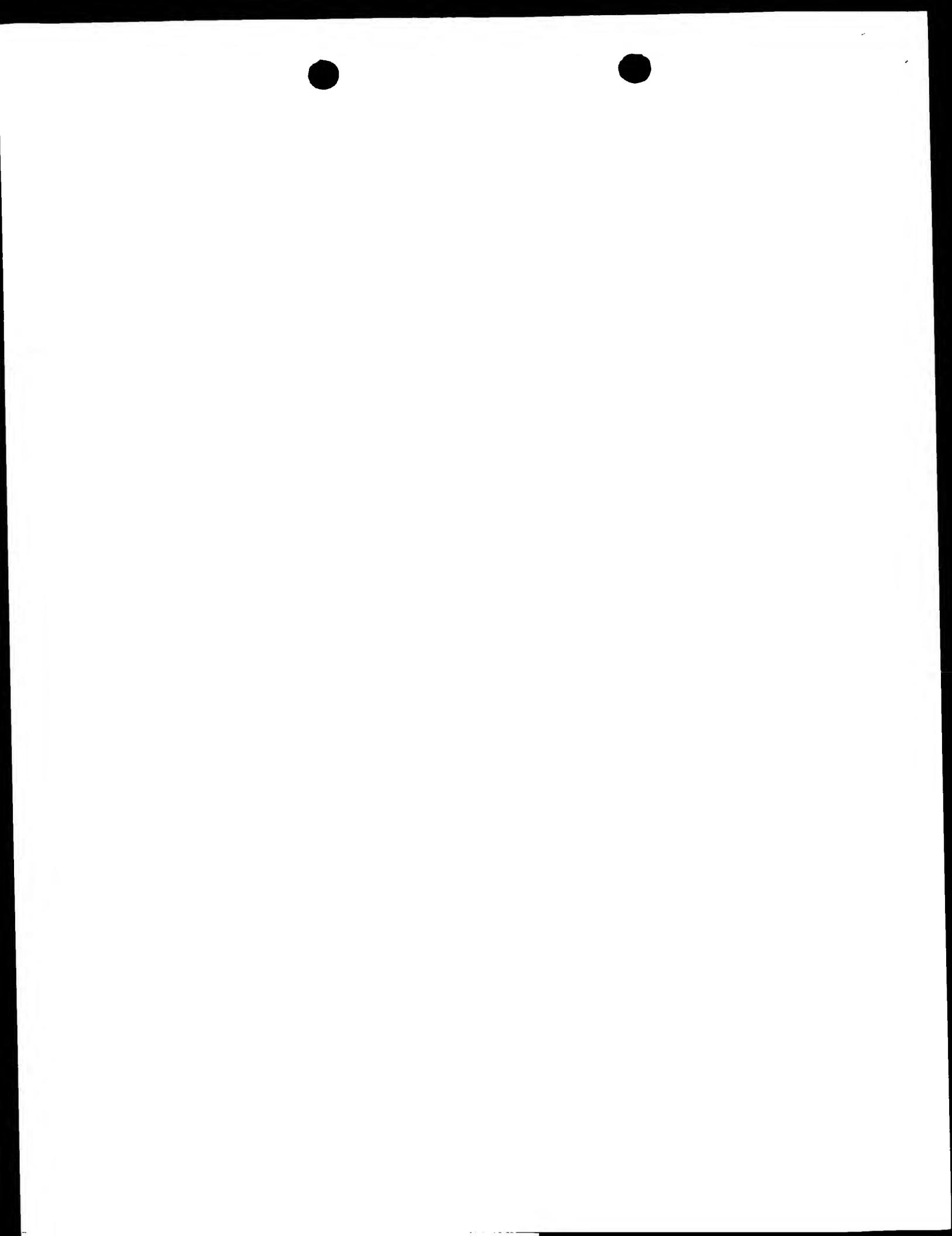
not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

all parts.

the parts relating to claims Nos. .



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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-6, 11-14, 19-25, 30-33, 38-49
	No: Claims 7-10, 15-18, 26-29, 34-37
Inventive step (IS)	Yes: Claims 1-6, 11-14, 19-25, 30-33, 38-49
	No: Claims 7-10, 11-14, 19-25, 30-33, 38-49
Industrial applicability (IA)	Yes: Claims 1-40, 43
	No: Claims

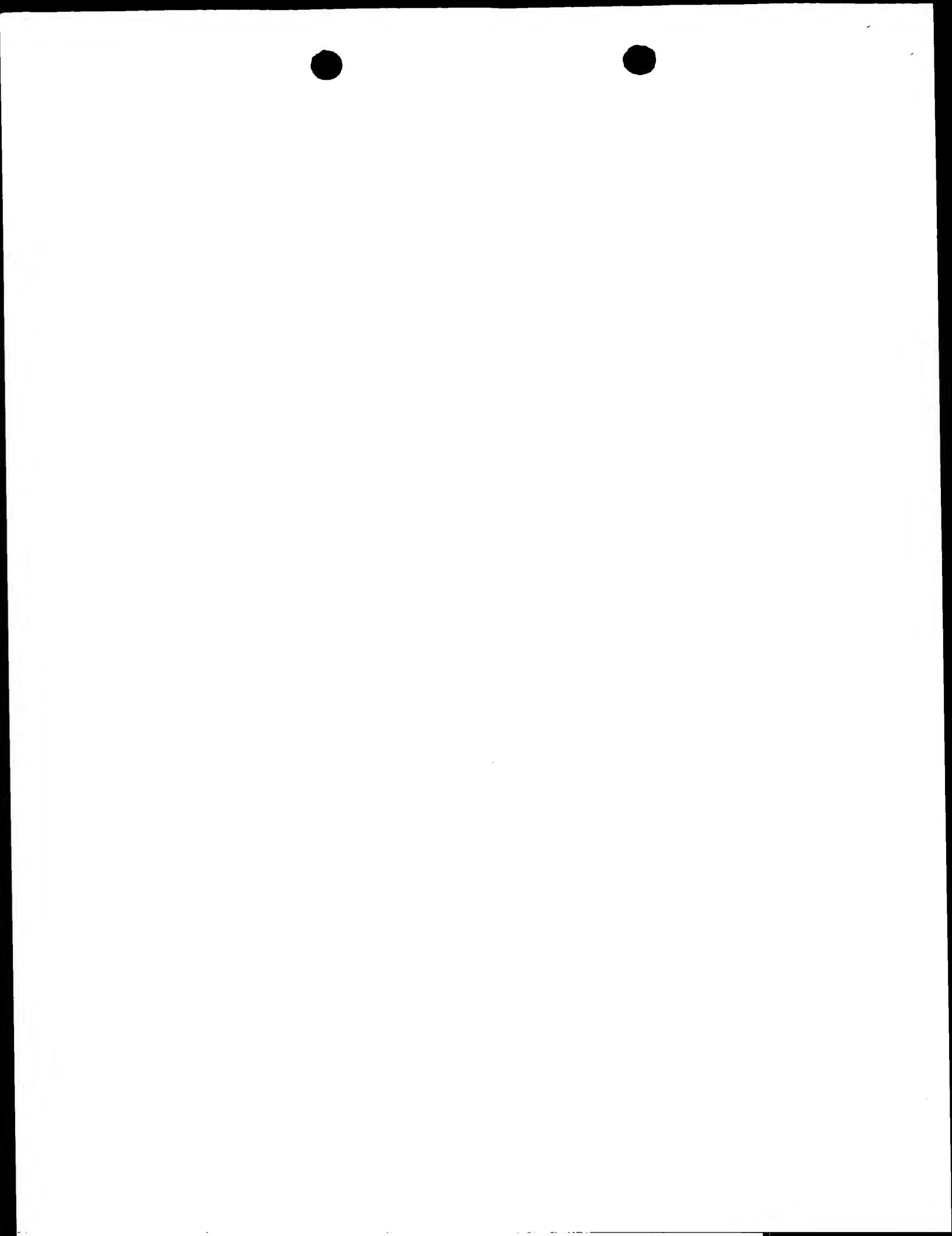
2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Novelty and Inventive step (Art. 33(2)(3) PCT)

The international preliminary examination is not being carried out on the part of Claims 44-48 referring to the therapeutic use of an agonist/antagonist of the polypeptide of Claim 1 or of Claim 20 because no search report has been established for this part of the claims due to insufficient characterization of their subject-matter (see ISR).

Industrial Applicability (Art 33 (4) PCT)

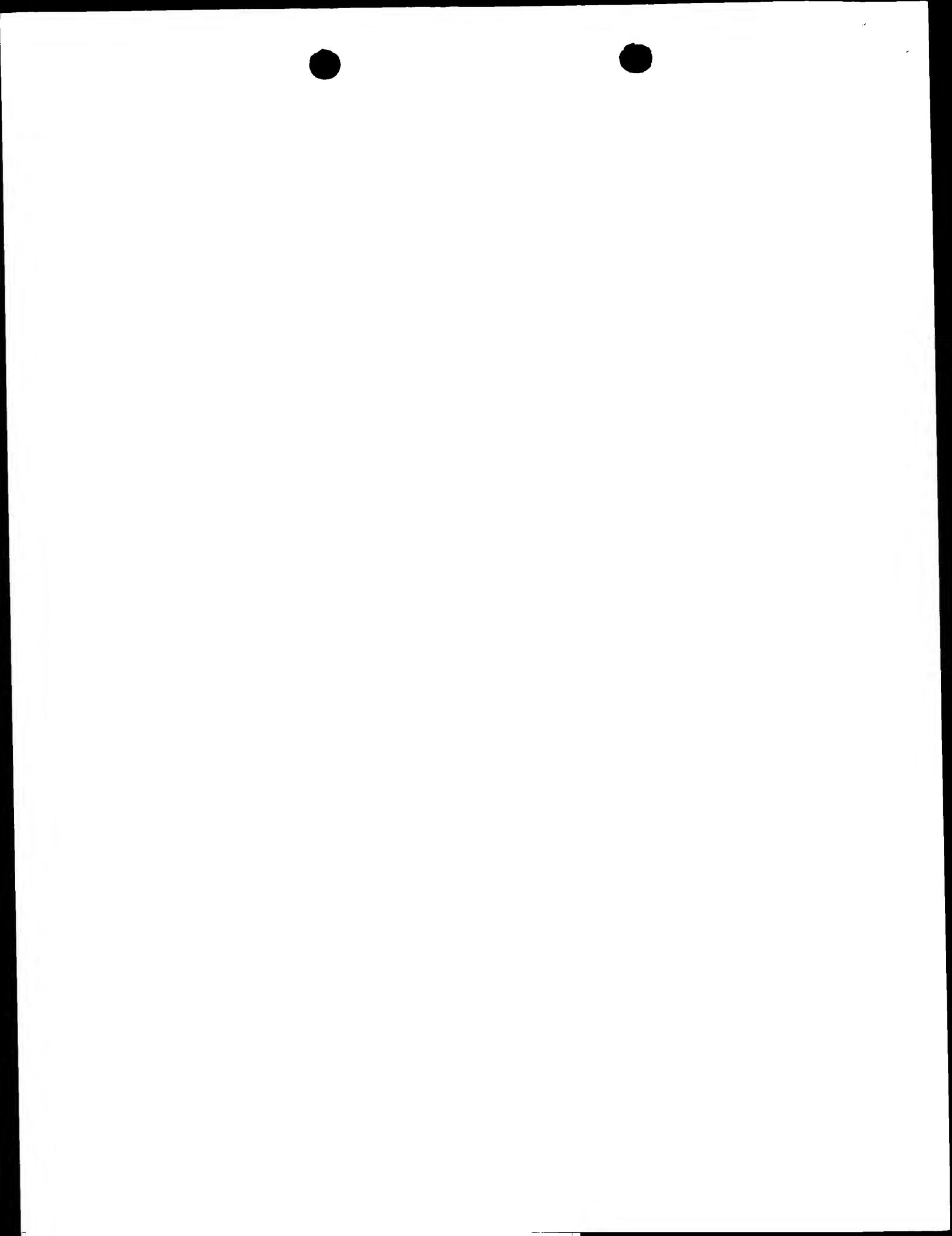
Claims 41, 42 and 44-49 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

For the assessment of the present Claims 41, 42 and 44-49, with regard to methods of treatment of the human/animal body, on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claim. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item IV

Lack of unity of invention

The ISA has found multiple inventions in this international application. However, as the ISA has provided a complete search report, the IPEA has decided not to invite the applicant to pay additional fees and to carry out the examination for all inventions.



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EXAMINATION REPORT - SEPARATE SHEET**

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The objection to lack of unity will, however, be prosecuted during regional phase examination at the EPO.

Re Item V

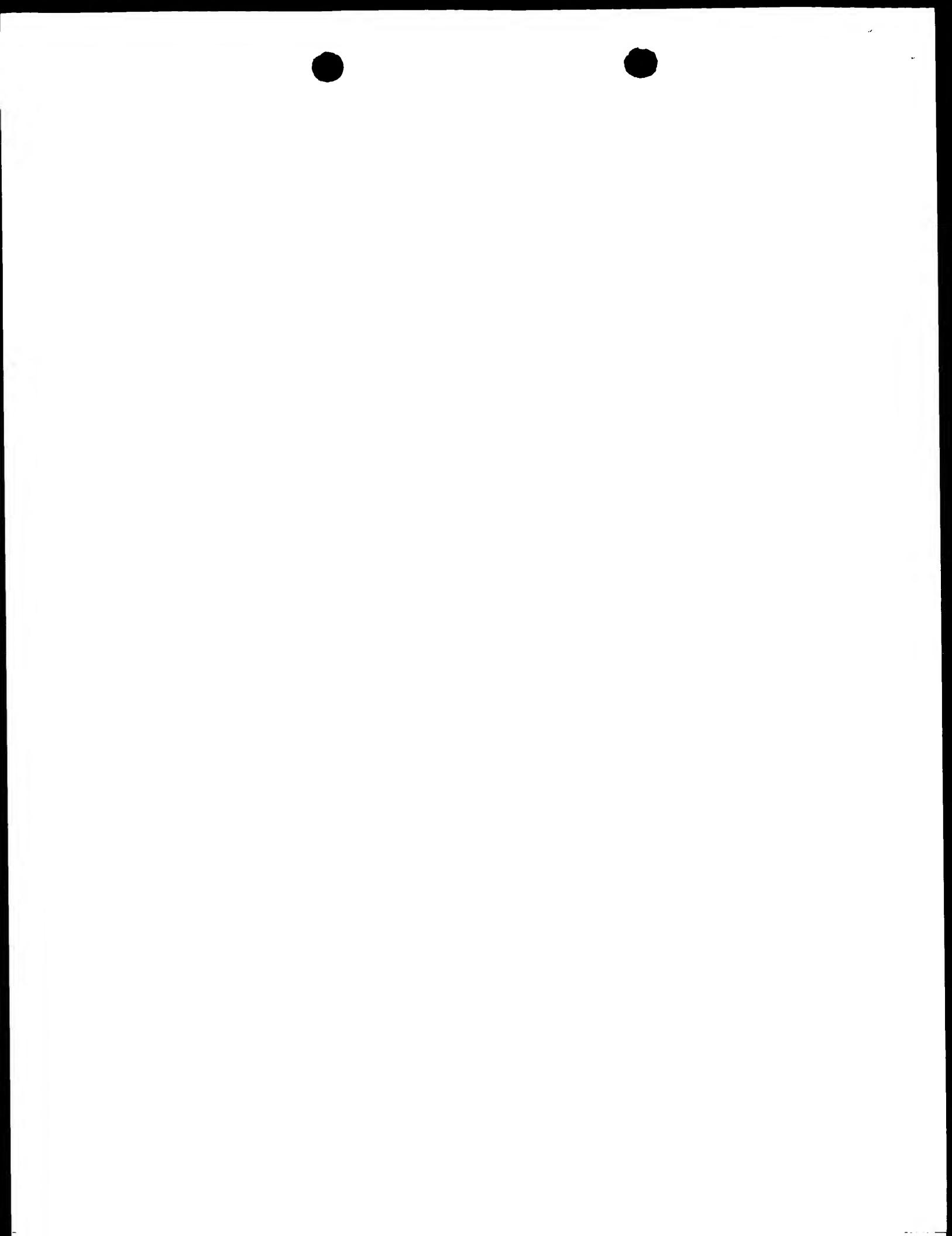
Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: DATABASE EMVRT [Online] E.M.B.L. Databases Accession Number: AF032118, 27 November 1997 (1997-11-27) YAMABHAI M ET AL: 'Intersectin, a novel adaptor protein with two eps15 homology and five src homology 3 domains' XP002117200 cited in the application -& YAMABHAI M ET AL: 'Intersectin, a novel adaptor protein with two Eps15 homology and five Src homology 3 domains' JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 273, no. 47, 20 November 1998 (1998-11-20), pages 31401-31407, XP002117205
- D2: WO 96 31625 A (CYTOGEN CORP ;UNIV NORTH CAROLINA (US)) 10 October 1996 (1996-10-10)
- D3: DATABASE EMEST24 [Online] E.M.B.L. Databases Accession Number: AA061808, 24 September 1996 (1996-09-24) MARRA M ET AL: 'Mus musculus cDNA clone 483558 5' similar to TR:G968973 G968973 EPS15R' XP002117201
- D4: DATABASE EMEST23 [Online] E.M.B.L. Databases Accession Number: AA217338, 11 February 1997 (1997-02-11) MARRA M ET AL: 'Mus musculus cDNA clone 652549 5' similar to SW:EP15_Mouse P42567 EPIDERMAL GROWTH FACTOR RECEPTOR SUBSTRATE 15' XP002117202

D1 discloses the DNA and amino acid sequence of Intersectin, a protein of *X. laevis* containing two EH and five SH3 domains. The sequences disclosed in D1 display 72.9% identity in 2129 bp overlap and 80.6% identity in 1216 aa overlap with Ese1.

D2 describes the cloning of SH3 domain-containing proteins. The proteins named SH3P17 and SH3P18 display identity with the SH3 domains of Ese1 and Ese2. The use of the



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DNAs encoding these proteins or fragments thereof as probes to identify further proteins is also disclosed, as well as antibodies recognizing these proteins.

D3 and D4 each disclose an EST similar to EPS15R with more than 90 % identity to the EH-containing domain of Ese1 and Ese2, respectively.

Novelty and Inventive step (Art. 33(2)(3) PCT)

1. Document D1 destroys the novelty of Claims 7, 9, 10, 15, 26, 29, and 34, as the nucleotide sequence it discloses comprises stretches of identity of at least 10 nucleotides with SEQ. ID. NO: 1, 4, 22 and 25, and the corresponding protein sequence comprises at least five consecutive amino acids of SEQ. ID. NO: 3, 6, 24 and 27. As the antigenic determinant of Claims 17 and 36 are not clearly defined (see also Item VIII, 3.), and in view of the degree of identity between Ese1(L) and Ese2(L) and Intersectin, the subject-matter of Claims 17 and 36 is also encompassed by the disclosure of D1.

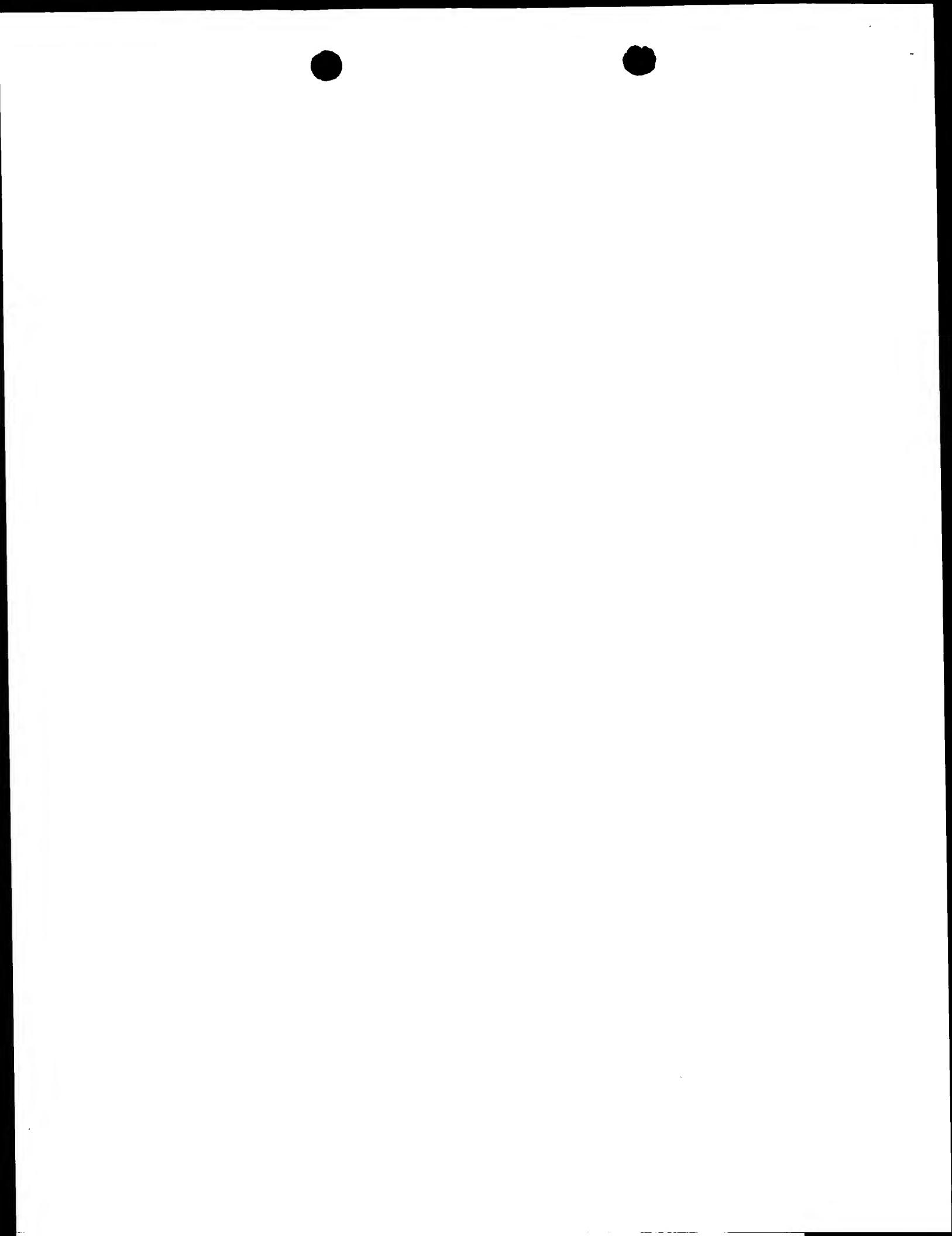
2. Document D2 destroys novelty of Claims 7-10, 15-18, 26-29 and 34-37. SEQ. ID. NO: 38 and 194 in D2 display, respectively, more than 5 consecutive amino acids identical to SEQ. ID. NO: 3 and 6 of the present application. The corresponding nucleic acid sequences display more than 10 consecutive nucleotides identity.

On page 63, lines 28-37, of D2 the use of these sequences as probes is disclosed. On page 74, 5.10, antibodies recognizing the proteins are disclosed.

3. The subject matter of Claims 1-4, 11-13, 19-23, 30-32, 38-43, 45-48 (partially, see Item III) and 49 could be considered novel and inventive if the objections raised in Item VIII, points 1 and 2 were overcome, as the subject-matter of the claims is not sufficiently defined.

Claims 5, 6, 14, 24, 25, 33 and 44 (partially, see Item III) are considered to be novel and inventive as proteins with the sequence of SEQ. ID. NO: 3, 6, 24 and 27, coded for by DNAs with the sequence of SEQ. ID. NO: 1, 2, 4, 5, 22, 23, 25, and 26, were not known or rendered obvious in the prior art.

The SH3 domain-containing proteins SH317 and SH318 disclosed in D2 are highly homologous to segments of Ese1 and Ese2 of the present application, but are not reported as containing EH-domains.



**INTERNATIONAL PRELIMINARY
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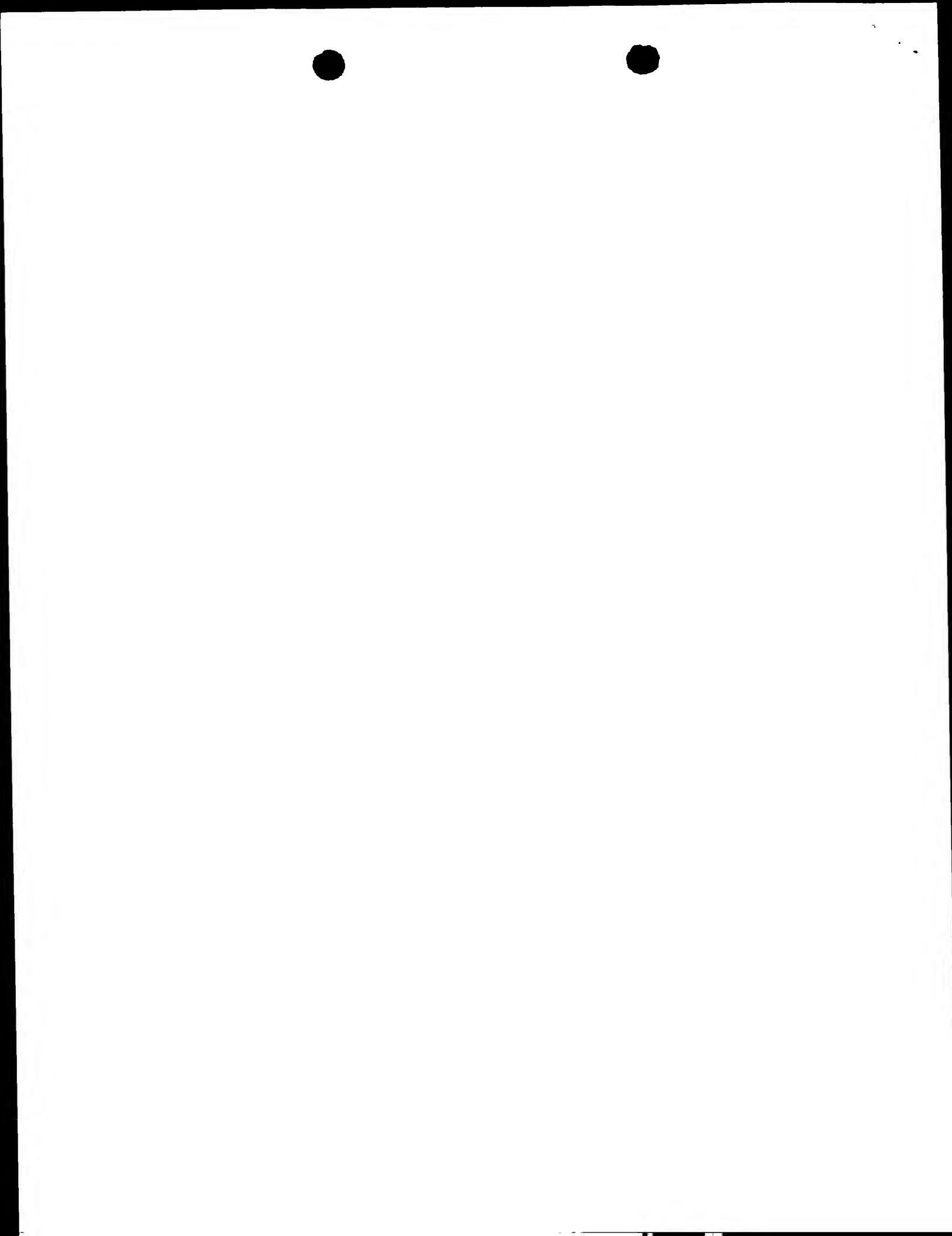
Pharmaceutical compositions to treat disorders involving abnormal endocytosis containing Ese proteins, methods of screening compounds useful in treating such disorders or methods of treatment of diseases characterized by abnormality in the endocytic pathway have also not been disclosed in the prior art.

The claims are considered to entail an inventive step although the prior art discloses the highly homologous protein Intersectin from *X. laevis* (D1), proteins with SH3 domains identical to those of Ese1(L) and Ese2(L) (D2) and ESTs with similarity to EPS15R containing EH domains and more than 90% identical to Ese1 and Ese2. The problem to be solved by the skilled person is seen as the identification and isolation of proteins with EH and SH3 domains involved in endocytosis. Starting from the available prior art, the skilled person would not have automatically arrived at the solution constituted by Ese1(L) and Ese2(L) as no link is evident between the proteins and DNAs of D2 and those of D3 and D4 which leads to the conclusion that the SH3 and EH domains might be part of the same protein(s). The existence of splice variants, in addition, would not have made it predictable that the skilled person would have isolated the claimed Ese1(L) and Ese2(L) proteins and DNA starting from the sequences published in D2-D4.

Re Item VIII

Certain observations on the international application

1. The designation "Ese1", "Ese1L", "Ese2" and "Ese2L" could not be found in any of the available prior art documents, which were published before the priority of the present application. Therefore this terminology is regarded as an internal designation. According to Rule 6.3 PCT, an invention should be defined in terms of its essential technical features. The characterization of a protein or DNA merely by an internal designation, which does not provide any technical teaching to the skilled person, is not considered sufficient to define unambiguously the matter for which protection is sought and therefore the application does not meet the requirements of Art. 6 PCT. Further characterizing features of the claimed protein or DNA that are necessary for the definition of the invention, such as its sequence, should be included in the claims.
2. The terms "allelic variant", "homologue", "fragment", "agonist" and "antagonist" found in Claims 4, 23, 39 and 44-48, without any structural or functional limitation are considered



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

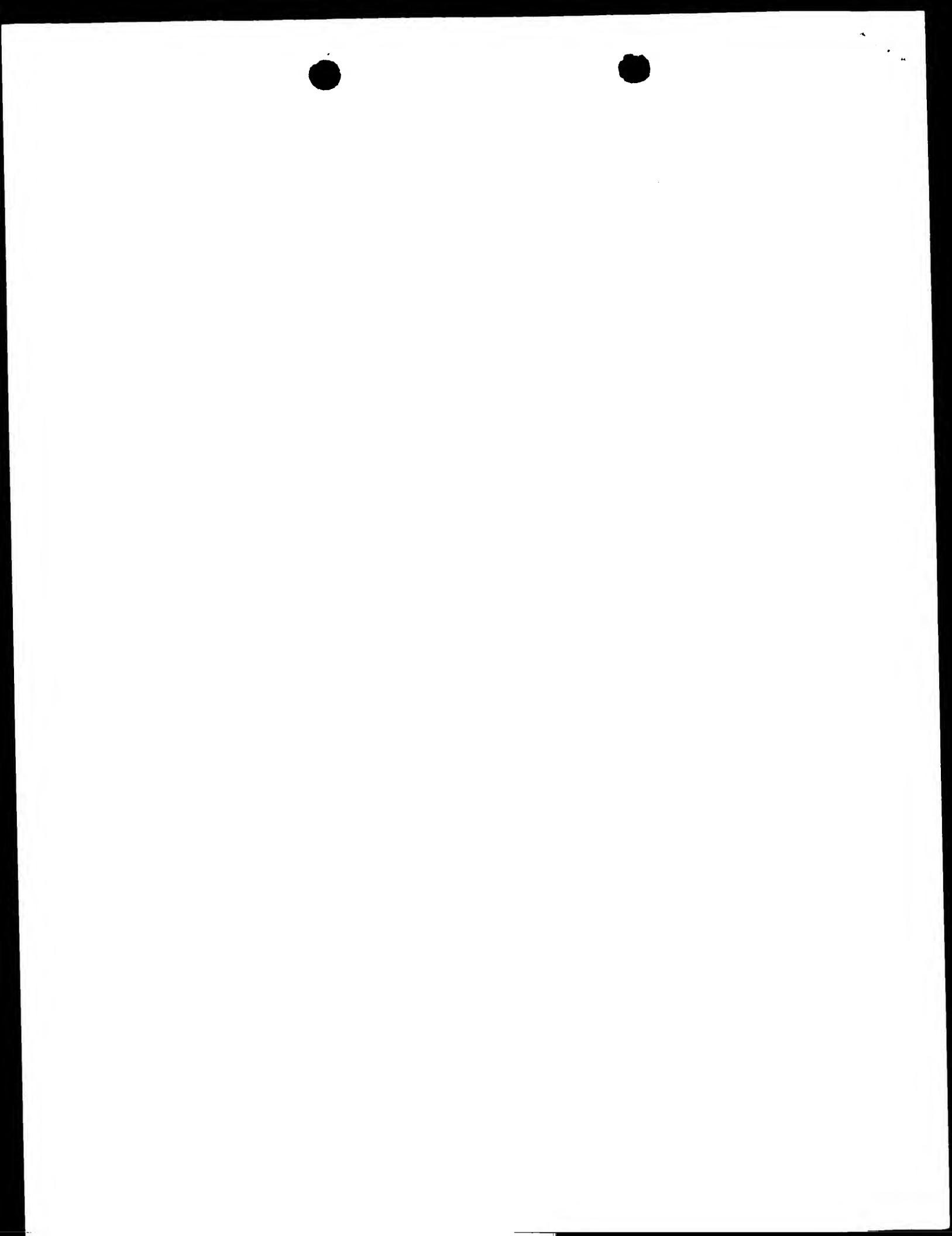
International application No. PCT/CA99/00375

to be vague and unclear as they leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the scope of the claims unclear and open to interpretation.

3. Claims 17 and 36 refer to polypeptides comprising an antigenic determinant of Ese1(L) or Ese2(L).

The subject-matter of the claims is unclear and not sufficiently disclosed in that the skilled person would not know how to select an antigenic determinant in Ese1(L) or Ese2(L) without undue burden on experimentation. Theoretically any fragment of five or more amino acids belonging to Ese1(L) or Ese2(L) could represent an antigenic determinant. The term "antigenic determinant" without any structural or functional limitation is vague and renders the scope of the claim unclear and open to interpretation. If an antibody reacting with Ese1(L) or Ese2(L), should cross-react with another, unrelated protein, this protein would be encompassed by the scope of the claim.

4. Claims 19 and 38 refer to a process for producing murine Ese1 and Ese 2 but are (also) dependent on Claims 3 and 22, relating to the DNA coding for human Ese1 and Ese2. This inconsistency should be corrected, as it renders the claims unclear.



PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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Sim & McBurney
330 University Avenue
6th floor
Toronto, Ontario M5G 1R7
CANADA

RECEIVED

AUG 8 2000

SIM & McBURNEY
SIM, HUGHES, ASHTON & MCKAY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year) 01.08.2000

Applicant's or agent's file reference
3206-169

IMPORTANT NOTIFICATION

International application No. PCT/CA99/00375	International filing date (day/month/year) 27/04/1999	Priority date (day/month/year) 27/04/1998
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Applicant
HSC RESEARCH AND DEVELOPMENT LIMITED...et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

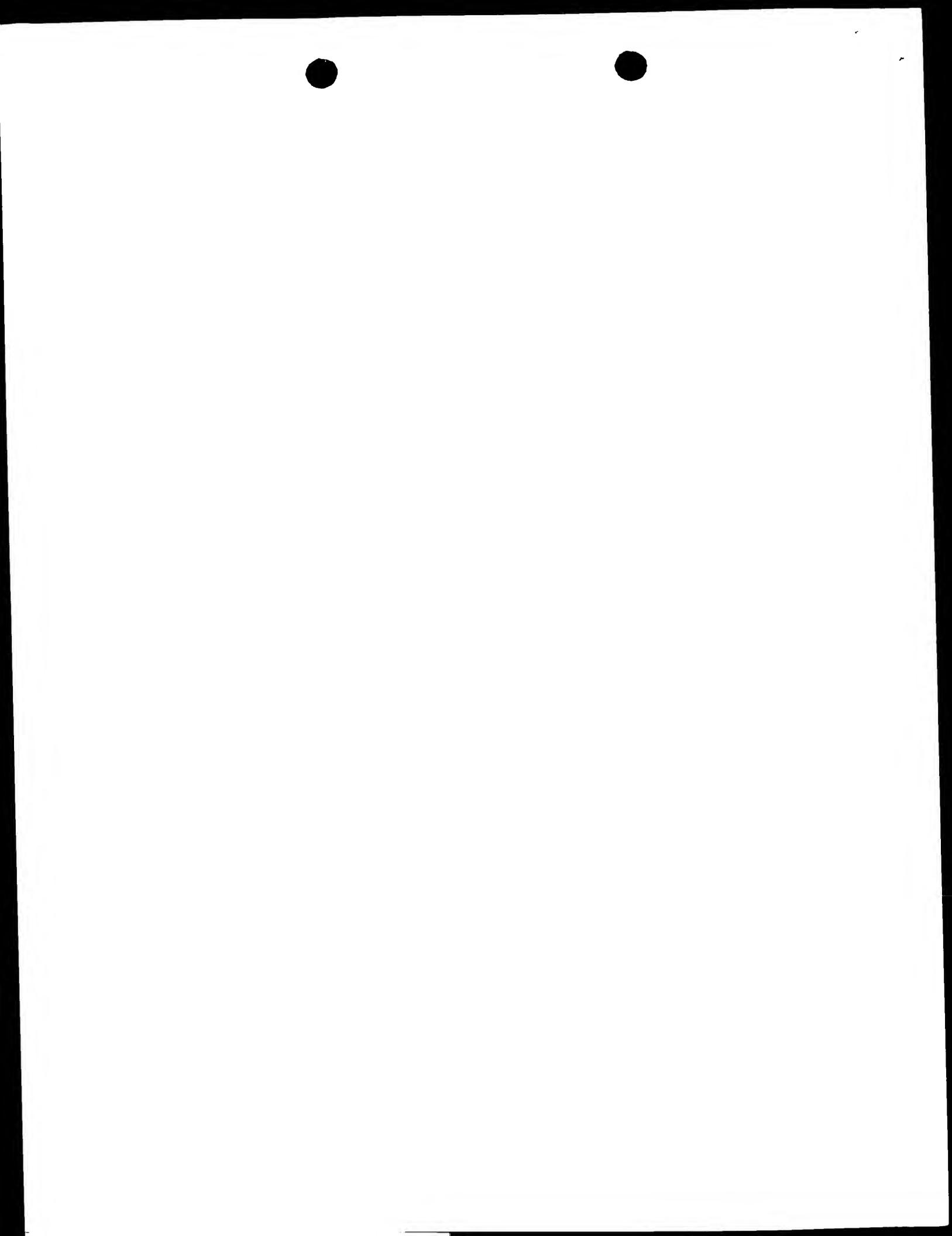
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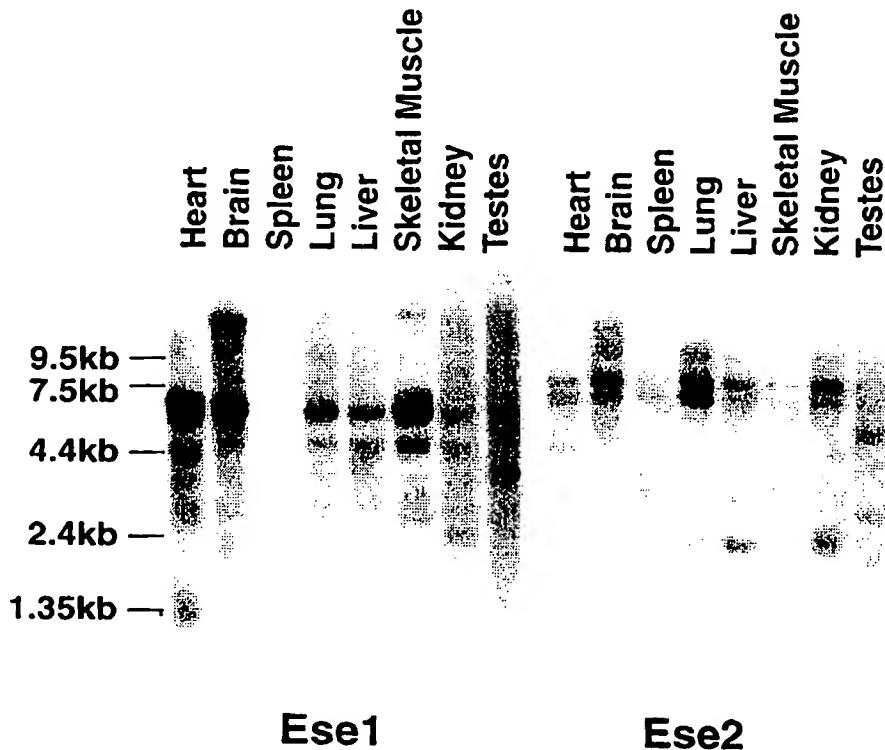


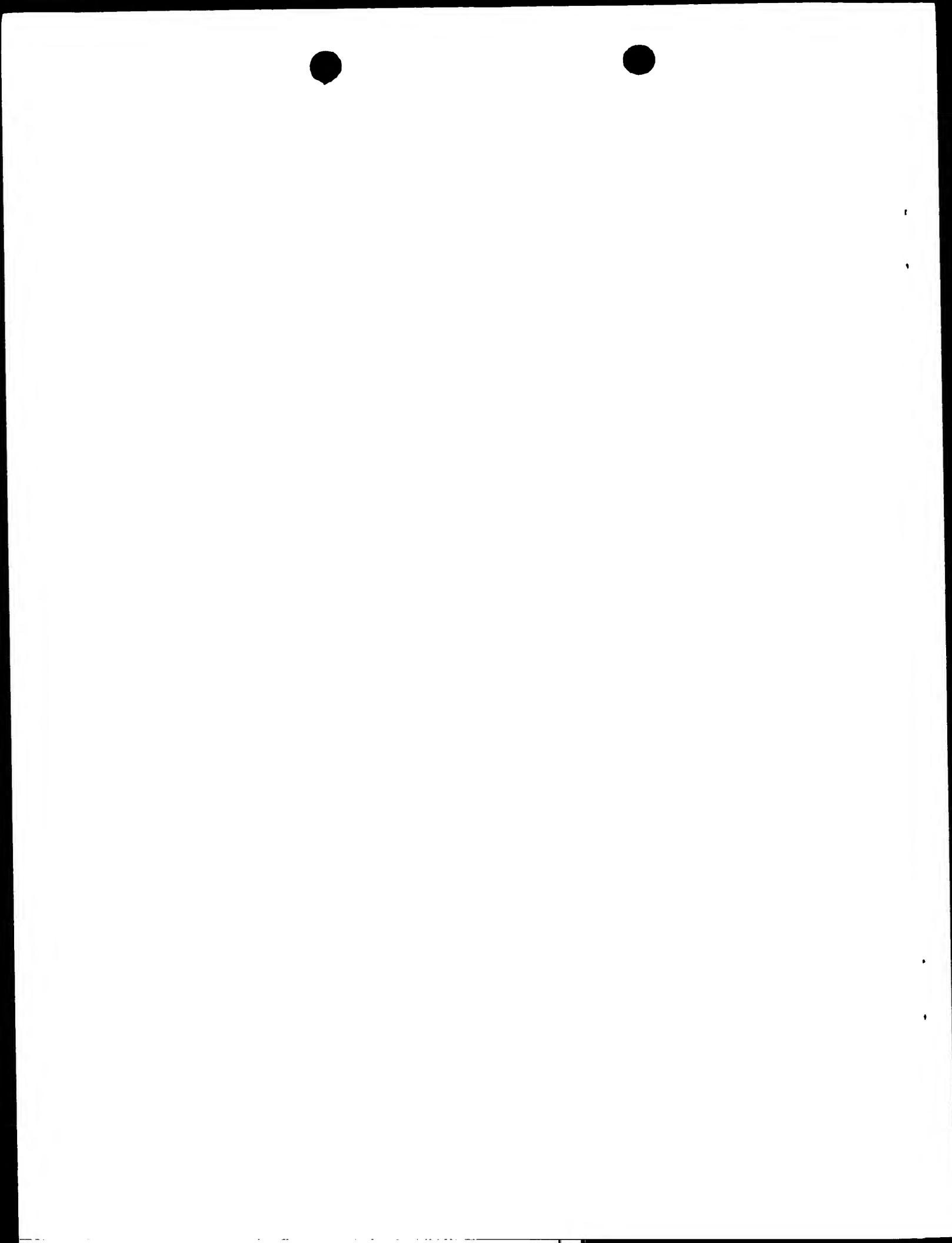
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/12, 5/10, 1/21, C07K 14/47, 16/18, A61K 31/70, 38/17, 48/00, G01N 33/50, C12Q 1/68		A3	(11) International Publication Number: WO 99/55728
			(43) International Publication Date: 4 November 1999 (04.11.99)
(21) International Application Number: PCT/CA99/00375			
(22) International Filing Date: 27 April 1999 (27.04.99)			
(30) Priority Data: 2,230,201 60/118,739	27 April 1998 (27.04.98) 5 February 1999 (05.02.99)	CA US	
(71) Applicant (for all designated States except US): HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP [CA/CA]; 555 University Avenue, Toronto, Ontario M5G 1X8 (CA).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(72) Inventors; and			
(75) Inventors/Applicants (for US only): EGAN, Sean, E. [CA/CA]; (CA). WANG, Wei [CA/CA]; (CA). SENGAR, Ameet [CA/CA]; The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8 (CA).			
(74) Agent: RAE, Patricia, A.; Sim & McBurney, 6th floor, 330 University Avenue, Toronto, Ontario M5G 1R7 (CA).			
(54) Title: ESE GENES AND PROTEINS			

(57) Abstract

The present invention describes the identification, isolation and characterization of novel mammalian proteins encoded by the Ese1 and Ese2 genes which are involved in endocytosis, vesicular trafficking and regulation of the actin cytoskeleton. Transcripts and products of these genes are useful for detecting abnormal cellular endocytosis processes as well as for developing assay systems to find and elucidate further binding partners of the proteins, to develop therapeutics to alter/restore protein function and for the isolation and manufacture of Ese proteins.

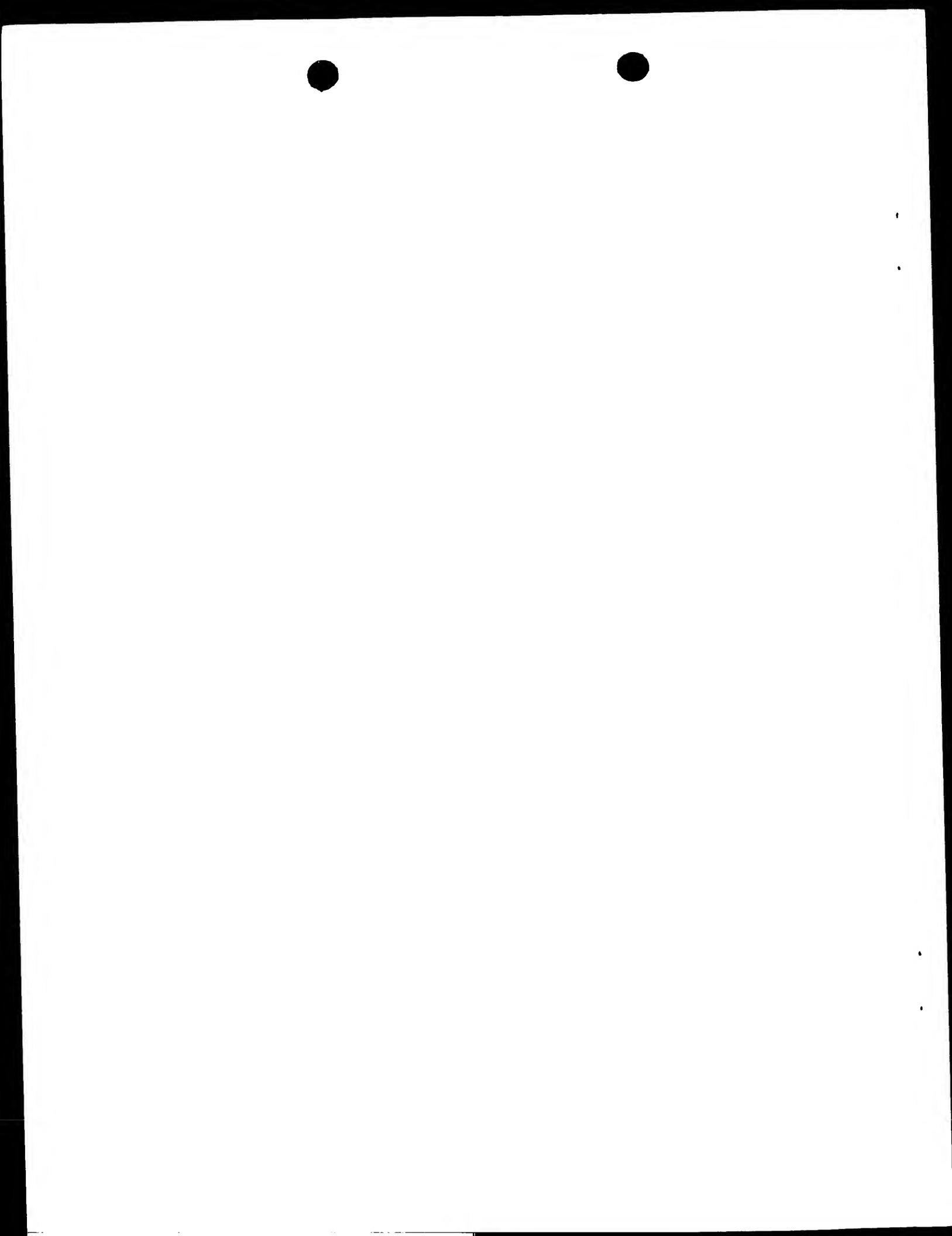




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EE	Estonia						



INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/00375

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6	C12N15/12	C12N5/10	C12N1/21	C07K14/47	C07K16/18
	A61K31/70	A61K38/17	A61K48/00	G01N33/50	C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMVRT E.M.B.L. Databases Accession Number: AF032118, 27 November 1997 (1997-11-27) YAMABHAI M ET AL: "Intersectin, a novel adaptor protein with two eps15 homology and five src homology 3 domains" XP002117200 cited in the application abstract	7-10, 26-29
P, X	-& YAMABHAI M ET AL: "Intersectin, a novel adaptor protein with two Eps15 homology and five Src homology 3 domains" JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 273, no. 47, 20 November 1998 (1998-11-20), pages 31401-31407, XP002117205 ---	7-10, 26-29

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

1 October 1999

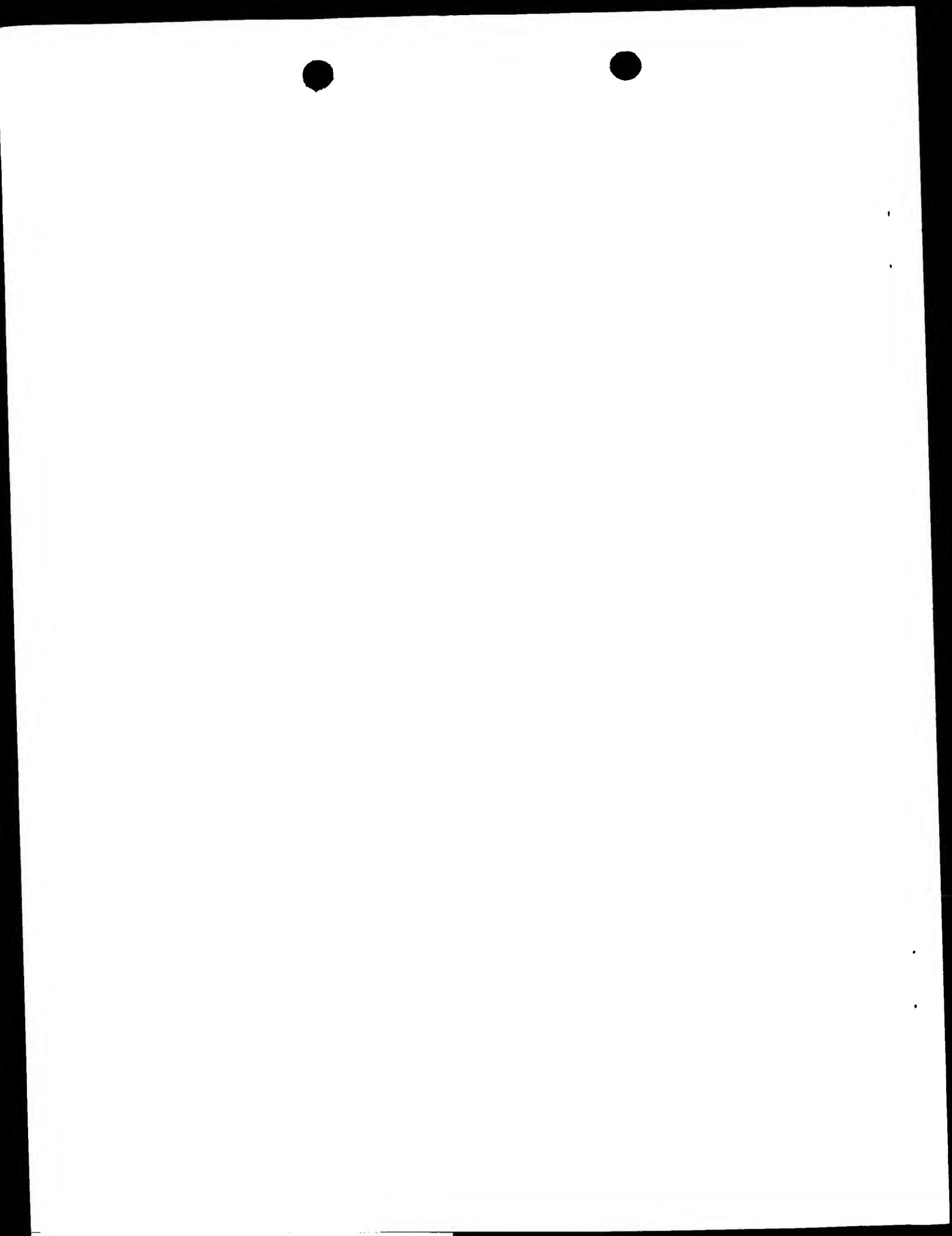
05/11/1999

Name and mailing address of the ISA

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Authorized officer

Lonnoy, O



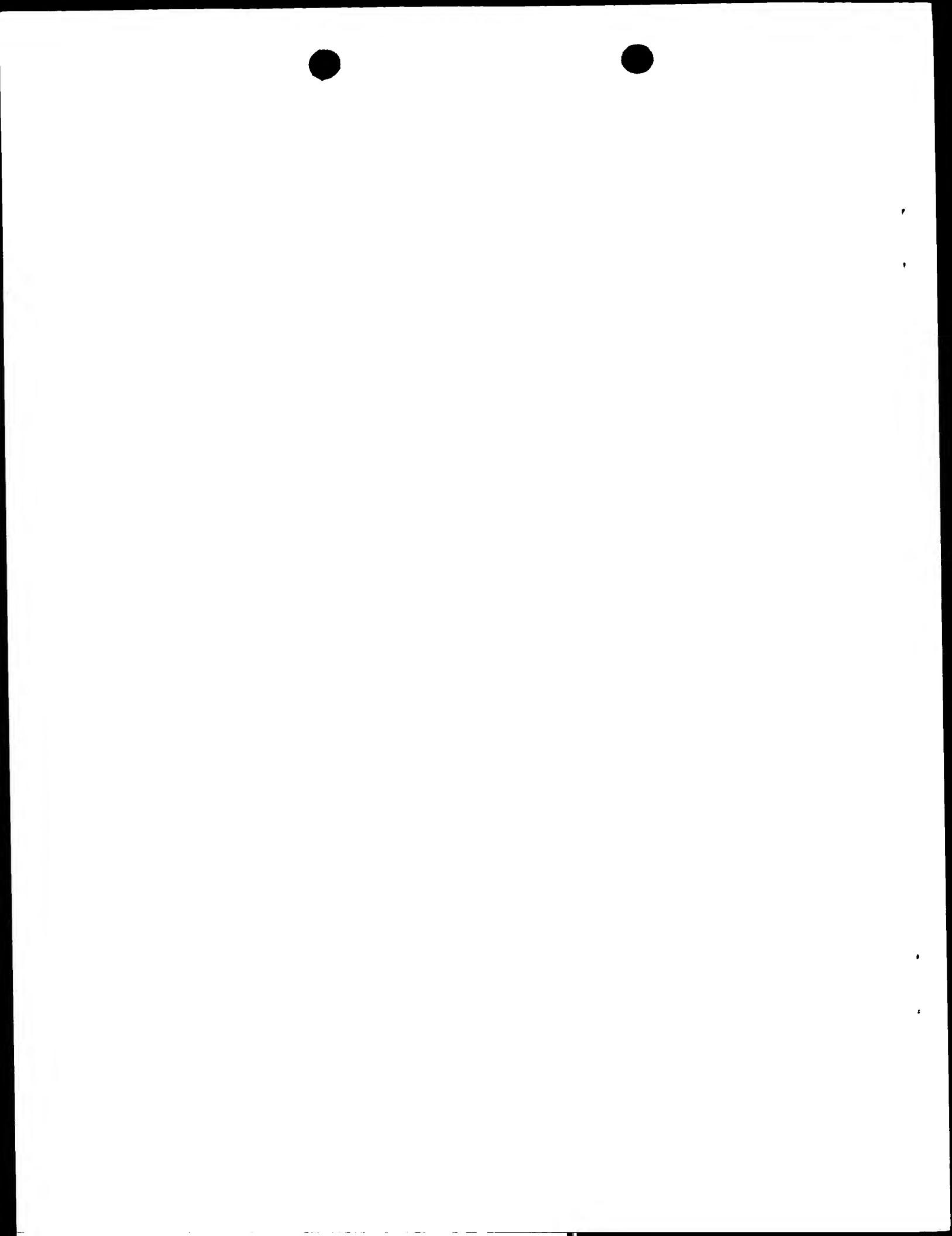
INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/00375

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 31625 A (CYTOGEN CORP ;UNIV NORTH CAROLINA (US)) 10 October 1996 (1996-10-10) Seq.Id.No.38; claims 75,79,99; "SH3P17" in Figure 9 and 10 / Seq.Id.No.194; claims 75,79,99; "SH3P18" in Figure 9 and 10 ---	7-10, 15-18, 26-29, 34-37
X	DATABASE EMEST24 E.M.B.L. Databases Accession Number: AA061808, 24 September 1996 (1996-09-24) MARRA M ET AL: "Mus musculus cDNA clone 483558 5' similar to TR:G968973 G968973 EPS15R" XP002117201 abstract ---	7,8
X	DATABASE EMEST23 E.M.B.L. Databases Accession Number: AA217338, 11 February 1997 (1997-02-11) MARRA M ET AL: "Mus musculus cDNA clone 652549 5' similar to SW:EP15_Mouse P42567 EPIDERMAL GROWTH FACTOR RECEPTOR SUBSTRATE 15" XP002117202 abstract ---	26,27
P,X	SENGAR A ET AL: "The EH and SH3 domain Ese proteins regulate endocytosis by linking to dynamin and Eps15" EMBO JOURNAL., vol. 18, no. 5, 1 March 1999 (1999-03-01), pages 1159-1171, XP002117197 figures 1,2,6 ---	1-38,48
P,X	GUIPPONI M ET AL : "Two isoforms of a human intersectin (ITSN) protein are produced by brain-specific alternative splicing in a stop codon" GENOMICS, vol. 53, no. 3, 1 November 1998 (1998-11-01), pages 369-376, XP002117198 figure 3 ---	1-19
A	US 5 717 067 A (FAZIOLI FRANCESCA ET AL) 10 February 1998 (1998-02-10) ---	1-49
	-/--	

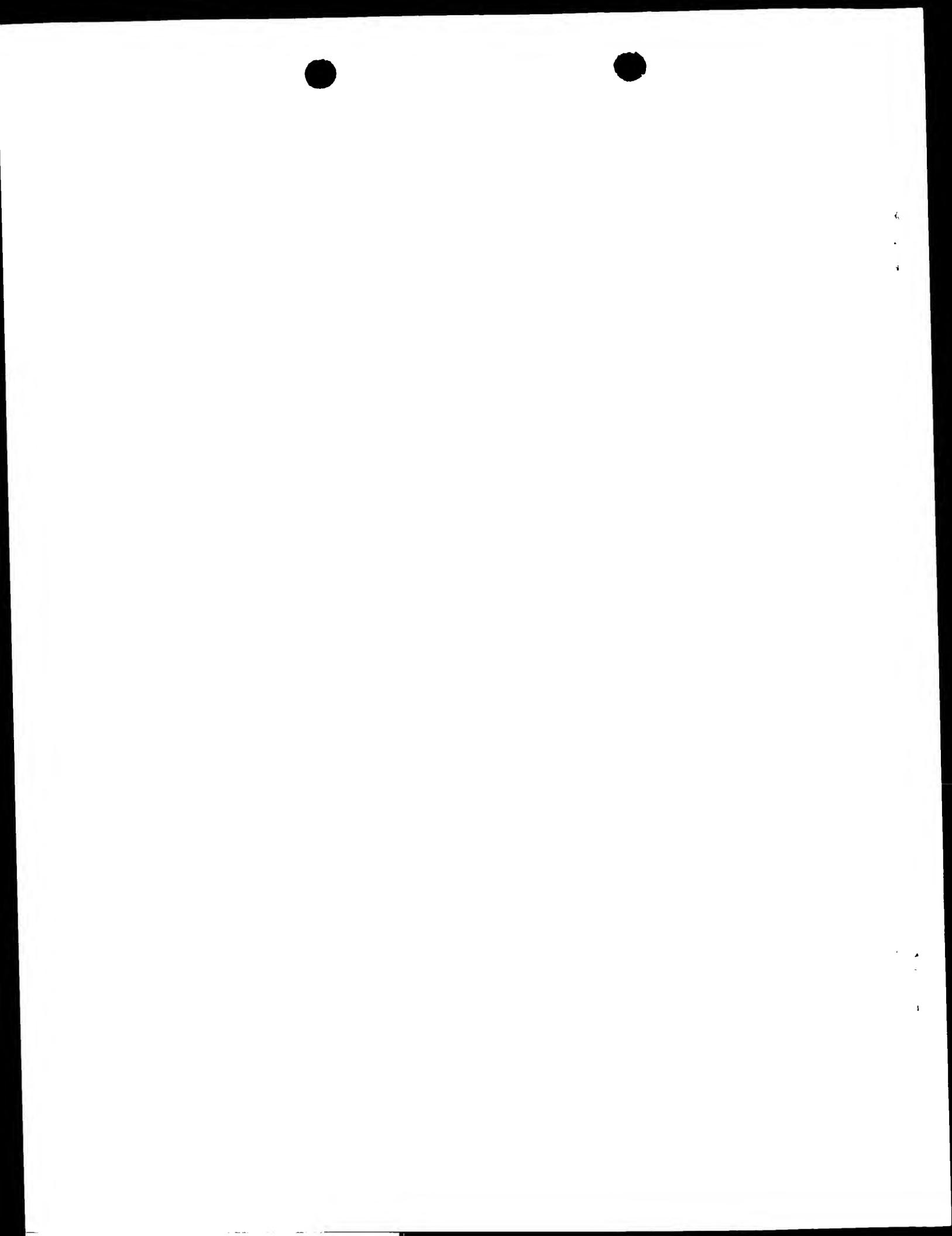


INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/00375

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9631625	A 10-10-1996	AU 5382196	A	23-10-1996	
		CA 2217641	A	10-10-1996	
		EP 0833941	A	08-04-1998	
		JP 11509172	T	17-08-1999	
		ZA 9602813	A	09-10-1996	
US 5717067	A 10-02-1998	US 5487979	A	30-01-1996	
		US 5378809	A	03-01-1995	
		US 5872219	A	16-02-1999	
		AU 4838093	A	15-03-1994	
		WO 9404571	A	03-03-1996	
		US 5610018	A	11-03-1997	



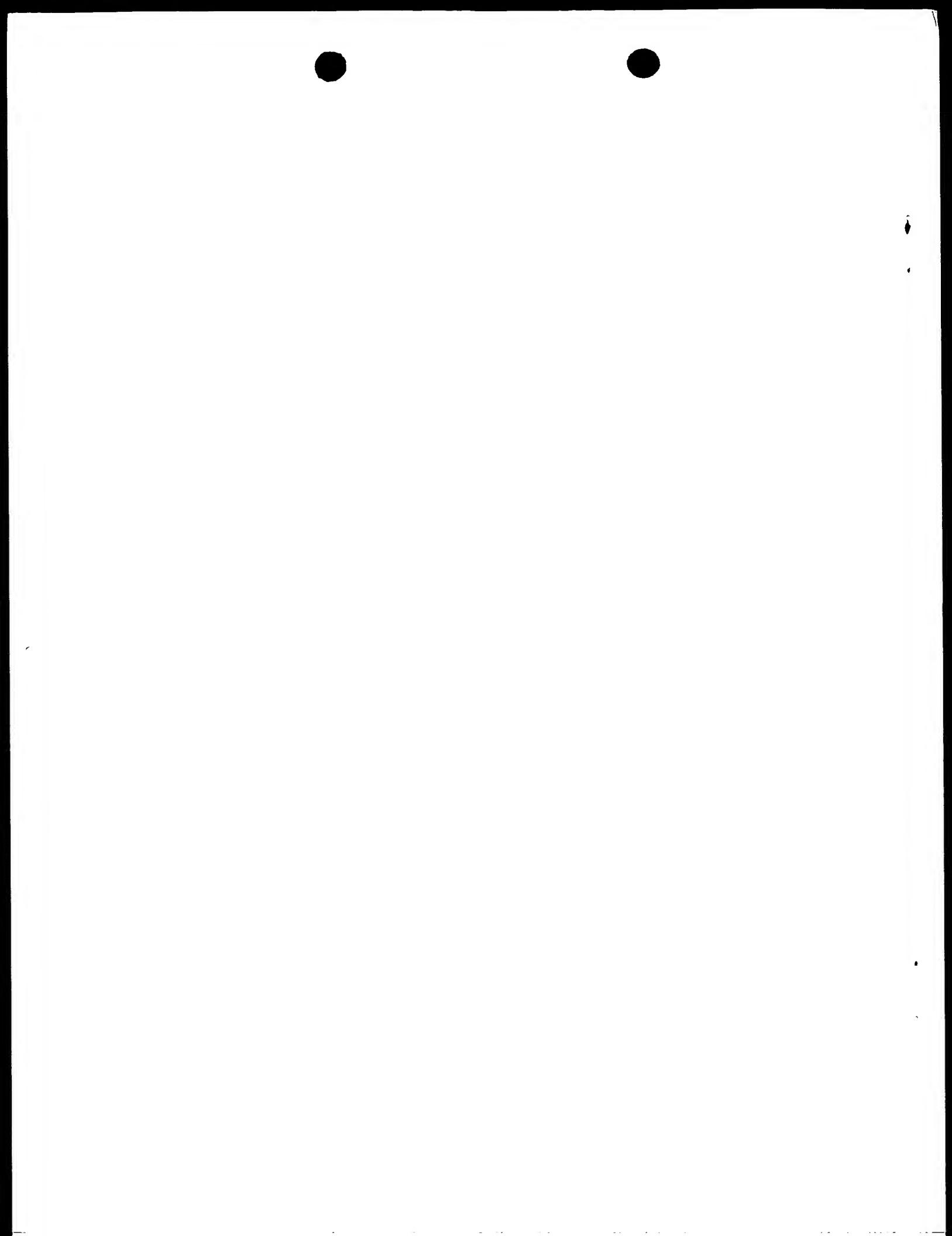
INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 99/00375

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SALCINI A ET AL: "Binding specificity and in vivo targets of the EH domain, a novel protein-protein interaction module" GENES & DEVELOPMENT, vol. 11, no. 17, 1 September 1997 (1997-09-01), pages 2239-2249, XP002117199 cited in the application -----	



INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA 99/ 00375

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 41, 42 and 44-49 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
See FURTEHR INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

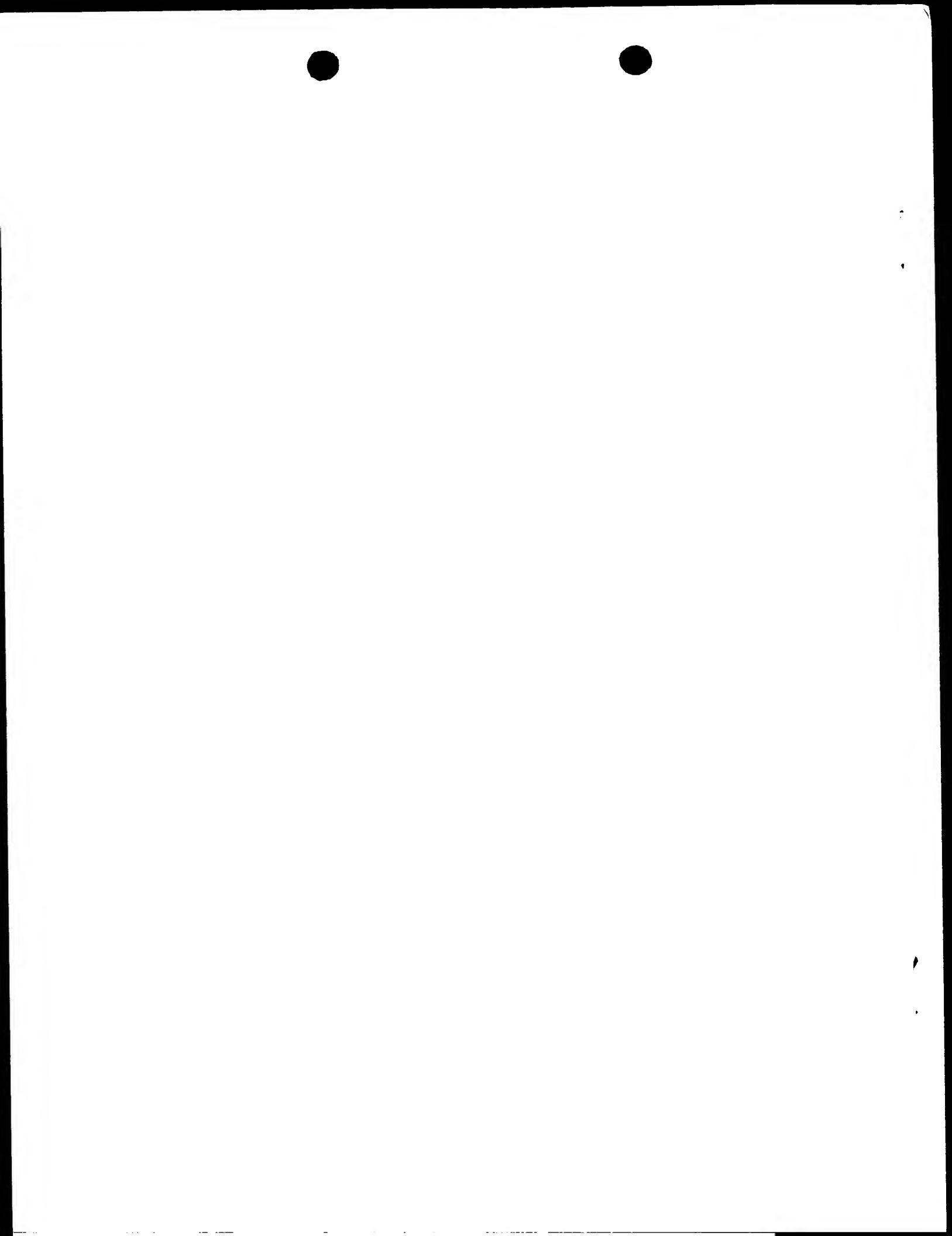
See additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19 and 39-49 (all partially)

An isolated nucleic acid comprising a nucleotide sequence encoding a mammalian Ese1 protein or a splice variant thereof; said nucleic acid of murine origin; said nucleic acid of human origin; said nucleic acid consisting of genomic DNA, cDNA or RNA; said nucleic acid encoding a protein comprising the amino acid sequence of Seq.Id.No.3; said nucleic acid comprising the sequence of Seq.Id.No.1 or Seq.Id.No.2; said nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides from Seq.Id.No.1 or Seq.Id.No.2; recombinant methods and products relating thereto; a substantially pure Ese1 protein; said protein of murine or human origin; said protein comprising the amino acid sequence of Seq.Id.No.3; a substantially pure polypeptide comprising at least 5 consecutive amino acid residues of Seq.Id.No.3; a substantially pure polypeptide comprising at least one functional domain of a mammalian Ese1 protein and an antibody which specifically bind to said polypeptide; a substantially pure polypeptide comprising at least an antigenic determinant of a mammalian Ese1 protein; diagnostic and therapeutic applications thereof.

2. Claims: 1-19 and 39-49 (all partially)

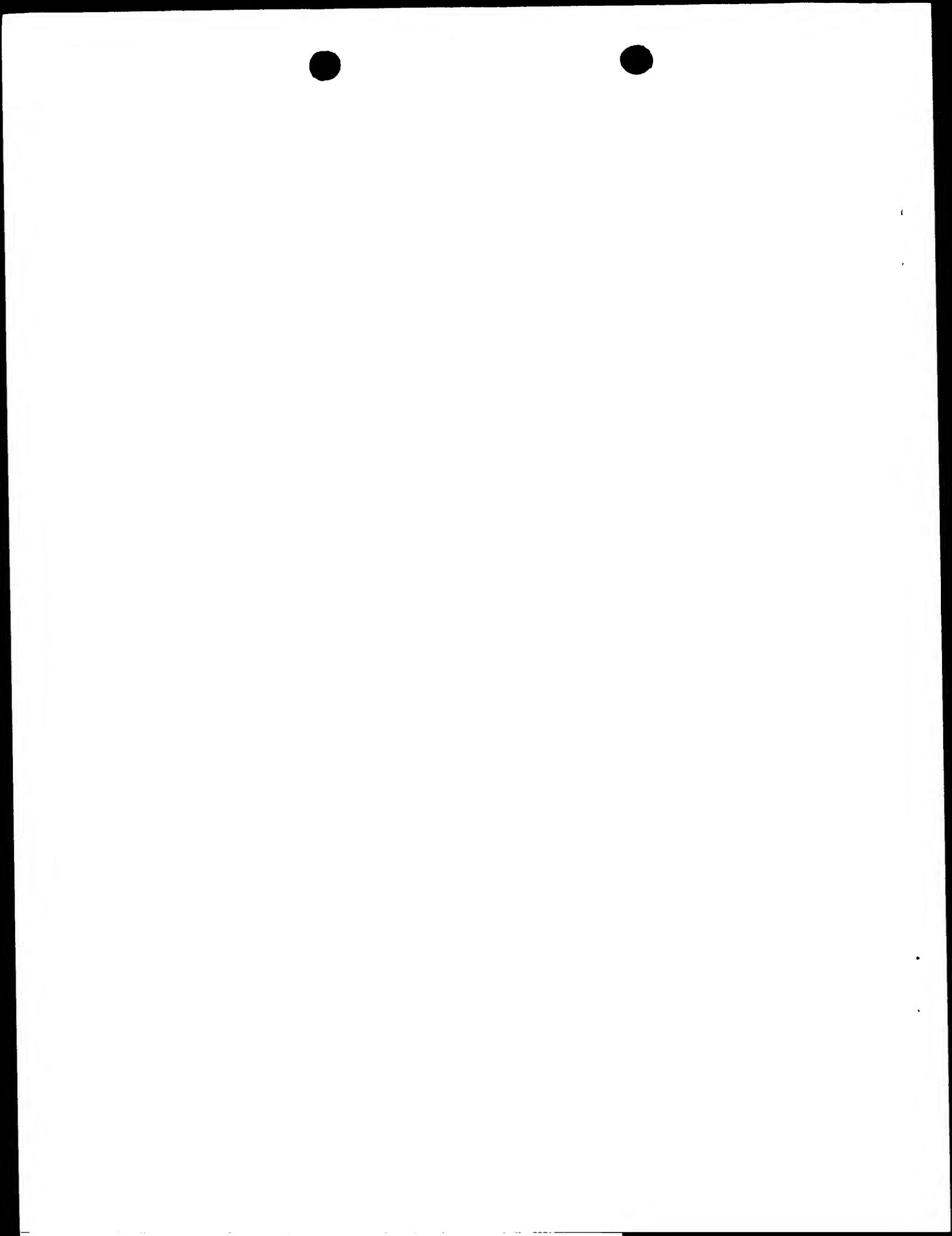
As for subject 1, but respectively relating to Ese1L; Seq.Id.No.24, Seq.Id.No.22, and Seq.Id.No.23.

3. Claims: 20-49 (all partially)

As for subject 1, but respectively relating to Ese2; Seq.Id.No.6, Seq.Id.No.4, and Seq.Id.No.5.

4. Claims: 20-49 (all partially)

As for subject 1, but respectively relating to Ese2L; Seq.Id.No.27, Seq.Id.No.25, and Seq.Id.No.26.

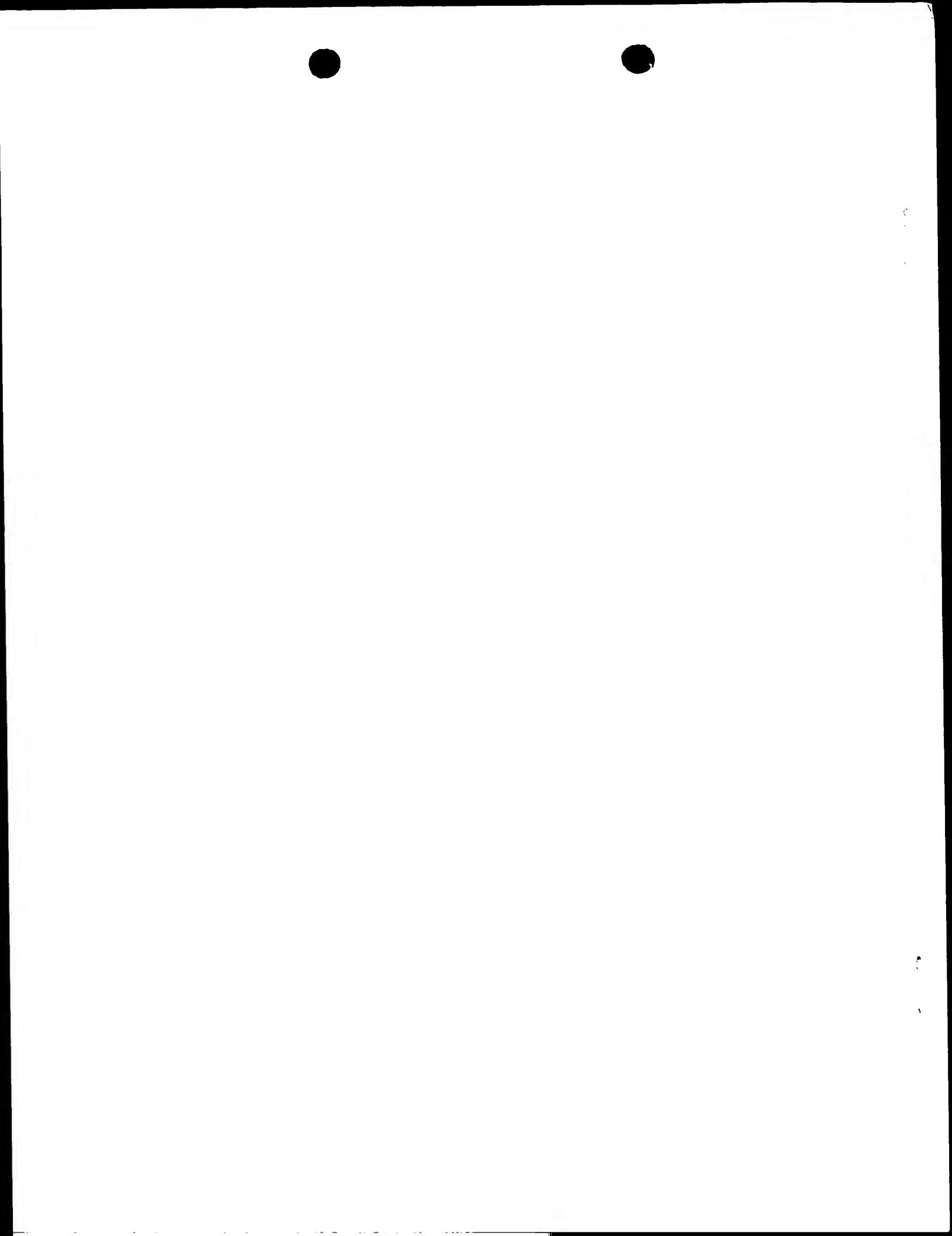


FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 44-48, relating to the therapeutic use of an agonist/antagonist of the polypeptide of claim 1 or of claim 20, could not be searched completely as their subject-matters were insufficiently disclosed.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 3206-169	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 99/ 00375	International filing date (day/month/year) 27/04/1999	(Earliest) Priority Date (day/month/year) 27/04/1998
Applicant HSC RESEARCH AND DEVELOPMENT LIMITED...et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

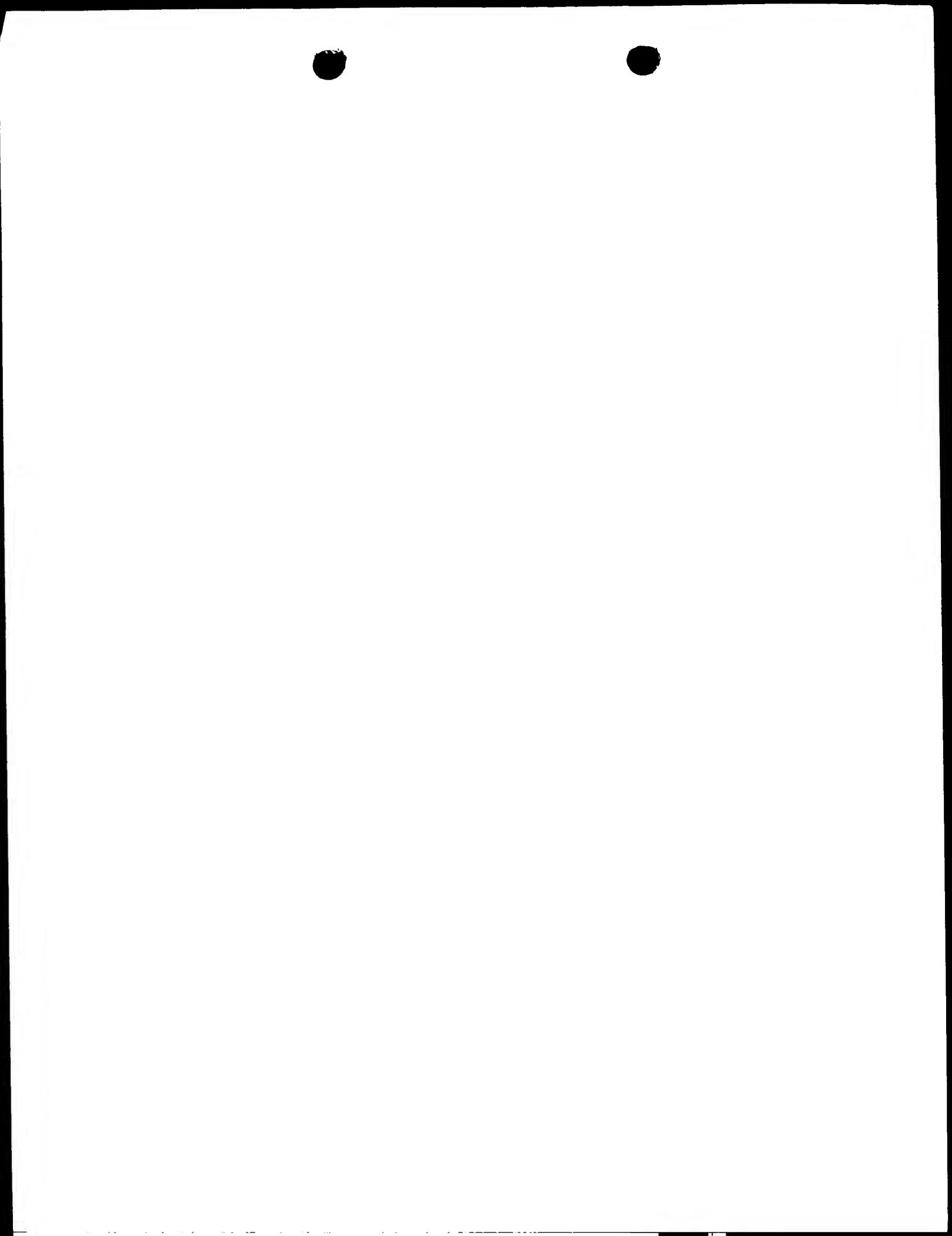
as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

2

None of the figures.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/04454

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/04454

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

435/6, 7.1, 7.5, 172.1, 240.1, 320.1; 530/300, 350, 387.9; 536/23.5

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN, DIALOG

search terms: library, gene expression, peptide, avidin, biotin, multiple antigen peptide, phage display, antibody, SH3, SH2, zinc finger, leucine zipper

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-52, 69-73, 89, 90 and 94-97 drawn to methods of identifying a polypeptide comprising a functional domain of interest.

Group II, claim(s) 53-68, 74, 75, 79, 80 and 101-102, drawn to a purified polypeptide, kits containing said purified polypeptide and methods of screening for a potential drug candidate.

Group III, claim(s) 76-78, 81-88 and 100 drawn to DNA encoding a polypeptide, a vector comprising said DNA, a recombinant cell and methods of producing a fusion protein.

Group IV, claim(s) 91-93, drawn to a method of determining the potential pharmacological activities of a molecule.

Group V, claim(s) 98 and 99, drawn to an antibody.

The inventions listed as Groups I-V do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The invention of Group I is drawn to a method of identifying a polypeptide comprising a functional domain of interest, and as claimed, does not require the products of Groups II, III and V. The polypeptide and kits of Group II have a defined seq. ID, which are not required in the method of Group I. In addition, functional domains such as SH3 domains are known in the art (see for Example, Cheadle et al., J. Biol. Chem. Vol. 269, No. 39, pages 24034-24039 (1994)). Further, the method of Group IV also lacks the technical feature of Group I as Group IV does not require the use of a multivalent recognition unit complex.

The invention of Group IV also does not have the same technical features as Groups II, III and V, as the method of Group IV as claimed does not require the products of Groups II, III and V. The polypeptide and kits of Group II have a defined seq. ID, which are not required in the method of Group IV. In addition, as stated above, functional domains such as SH3 domains are known in the art.

Groups II and III also lack a single concept. Group II is drawn to polypeptide and Group III is drawn to DNA, and thus have different structure and function. In addition, as stated above, polypeptides comprising functional domains such as SH3 domains are known in the art. Group V also does not relate to a single inventive concept, as Group V is drawn to an antibody, and is not required by the method of Groups I or IV, and is a separate product than the products of Groups II and III, having a different function and structure.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA 99/00375

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 41, 42 and 44-49

are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2.

Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

See FURTEHR INFORMATION sheet PCT/ISA/210

3.

Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

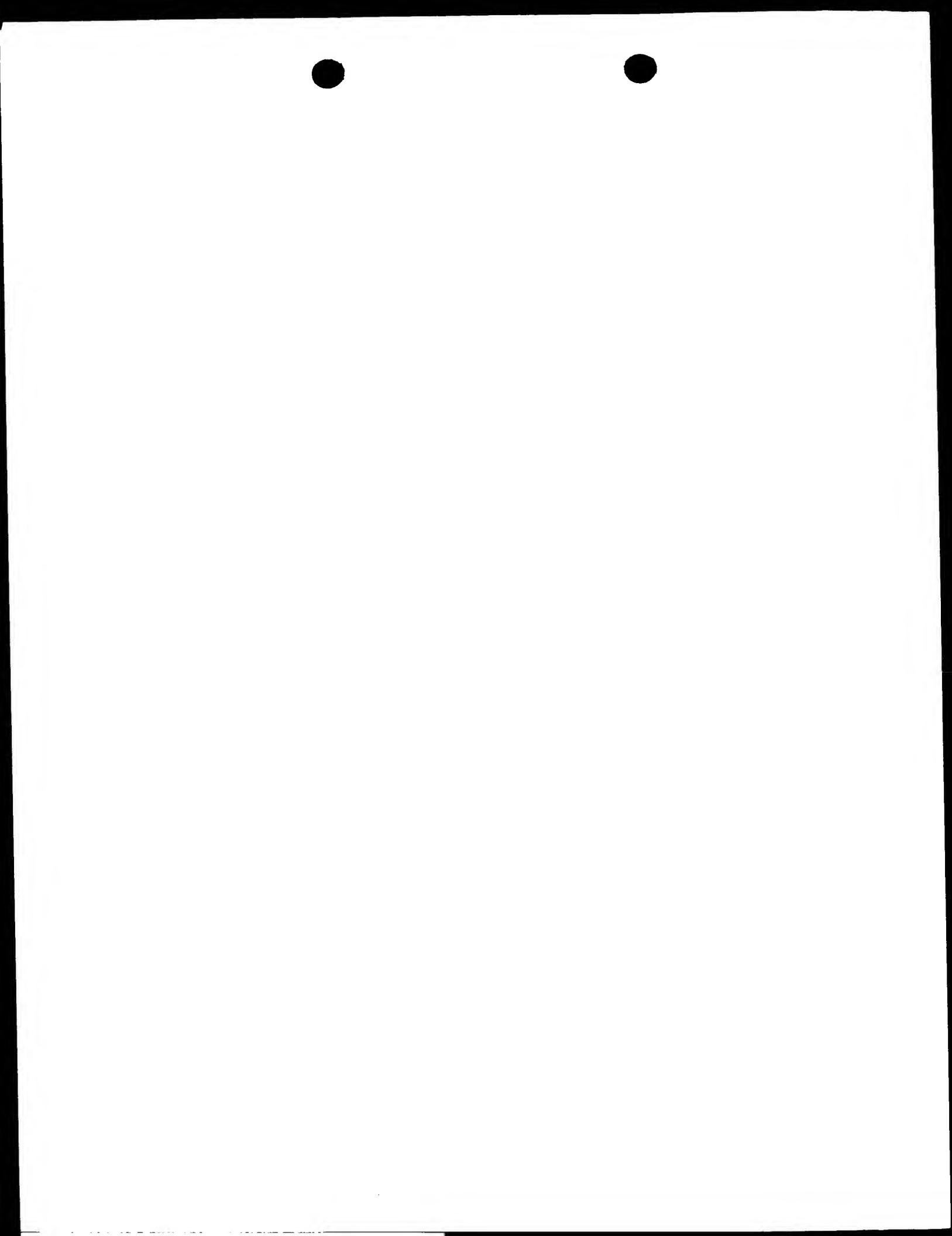
See additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19 and 39-49 (all partially)

An isolated nucleic acid comprising a nucleotide sequence encoding a mammalian Ese1 protein or a splice variant thereof; said nucleic acid of murine origin; said nucleic acid of human origin; said nucleic acid consisting of genomic DNA, cDNA or RNA; said nucleic acid encoding a protein comprising the amino acid sequence of Seq.Id.No.3; said nucleic acid comprising the sequence of Seq.Id.No.1 or Seq.Id.No.2; said nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides from Seq.Id.No.1 or Seq.Id.No.2; recombinant methods and products relating thereto; a substantially pure Ese1 protein; said protein of murine or human origin; said protein comprising the amino acid sequence of Seq.Id.No.3; a substantially pure polypeptide comprising at least 5 consecutive amino acid residues of Seq.Id.No.3; a substantially pure polypeptide comprising at least one functional domain of a mammalian Ese1 protein and an antibody which specifically bind to said polypeptide; a substantially pure polypeptide comprising at least an antigenic determinant of a mammalian Ese1 protein; diagnostic and therapeutic applications thereof.

2. Claims: 1-19 and 39-49 (all partially)

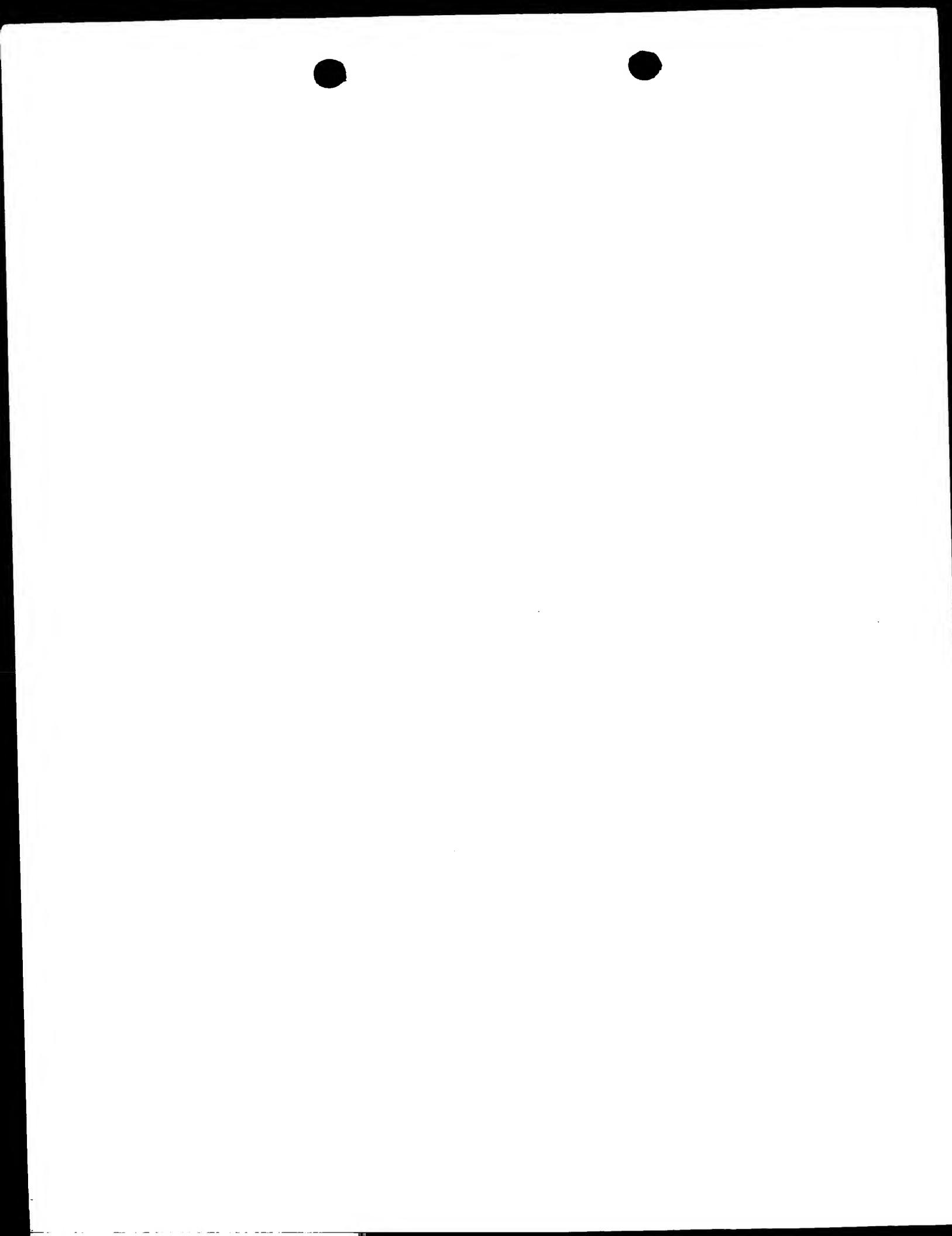
As for subject 1, but respectively relating to Ese1L; Seq.Id.No.24, Seq.Id.No.22, and Seq.Id.No.23.

3. Claims: 20-49 (all partially)

As for subject 1, but respectively relating to Ese2; Seq.Id.No.6, Seq.Id.No.4, and Seq.Id.No.5.

4. Claims: 20-49 (all partially)

As for subject 1, but respectively relating to Ese2L; Seq.Id.No.27, Seq.Id.No.25, and Seq.Id.No.26.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 44-48, relating to the therapeutic use of an agonist/antagonist of the polypeptide of claim 1 or of claim 20, could not be searched completely as their subject-matters were insufficiently disclosed.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

